

# Sanocrysin in the Treatment of Pulmonary Tuberculosis.

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## Section 1.

### Introduction.

Innumerable remedies have been employed in the treatment of tuberculosis ever since the disease was first recognised, but very few have stood the test of time.

The modern treatment of pulmonary tuberculosis has resolved itself into three lines of action, viz.,

1. Building up the tissue resistance to the infecting organism. Open air and sanatorium treatment have found their place in fulfilling this function, and have now become established routine through many years of experience.

2. Surgical Treatment. Collapse therapy, which embraces artificial pneumothorax, thoracoplasty and phrenic avulsion, is now accepted as invaluable treatment for selected cases. The aim of these surgical procedures is immobilisation of the affected lung in order to give the lesions an opportunity to heal.

3. Chemotherapy. The search for a specific for tuberculosis has gone on through the ages, stimulated at intervals by the work of such men as Ehrlich and Koch. The stimulus given to chemotherapy by the successful treatment of protozoal infections, encouraged workers on the subject to look for a similar specific for tuberculosis. Amongst the heavy metals gold had attracted considerable attention, till Moellgaard in 1924 claimed that in sanocrysin, a preparation of gold, he had found a specific remedy for the treatment of tuberculosis.

An attempt will be made in this thesis, to review the history of the gold treatment of tuberculosis, to outline the experimental work with sanocrysin particularly Moellgaard's pioneer work, and to assess the results obtained in 22 cases of pulmonary tuberculosis treated with this gold salt.

History of Gold Therapy of Tuberculosis.

The earliest record of the use Gold as a therapeutic agent dates back to the 8th century, when Abu Moussa the Wise recommended it as a cure for every known disease(1).

Paracelsus, (2) in 1500 A.D. used gold in combination with mercury in the treatment of Tuberculosis and it is recorded that physicians of that time used gold in the treatment of various cachexias resulting from phthisis, scrofula and syphilis (3), but on account of serious accidents it lapsed into disuse.

In 1810, Christien (4) reintroduced gold in the form of the chloride, considering this to be the most efficacious and reliable salt. Orfila (1818) Tallemant (1822), Werdt (1824), Le Grand (1837) Pitcairn and Neligan (1844) and many others took part in this revival of chemotherapy, and used gold preparations in the treatment of phthisis, scrofula, scirrhus indurations and glandular enlargements; Majendie (1838) used a cyanurate of gold, while M. Pourché considered the cyanide to be quite efficacious, though milder in action than the chloride.

These earlier attempts at chemotherapy with heavy metals were purely empirical; the results were variable and confusing, and, it was not until the end of the nineteenth, and beginning of the twentieth centuries, that the chemotherapeutic measures were directed on a more rational and sound basis. The modern chemotherapeutic movement was initiated by Paul Ehrlich of Frankfurt (1854 - 1915). He realised that antibodies were nature's defence mechanism against infection; that they were strongly antagonistic to the parasitic organism,



and quite harmless to the host. Attempts were then made to find a synthetic preparation of maximal 'parasitropic' and minimal 'organotropic' properties. "In the strictest sense, the sense of Ehrlich, chemotherapy has to do with drugs, which, in non-lethal doses, are able to kill all the specific disease organisms in the body at a single dose - the 'magna sterilans' action of Ehrlich; a chemical disinfection of the living body" (5). This implies a specific affinity of the chemical compound employed for the parasite in question, i.e., it must be bactericidal.

In the search for a specific for Tuberculosis the salts of gold and copper attracted most attention. In 1885 A. Luton began to treat Tuberculosis with various compounds of copper, and in 1894 his son, Ernest Luton, published a monograph on the results (6). Grafen Von Linden published results to show that subcutaneous injections of  $\text{Cu Cl}_2$  had a marked protecting influence on infected animals; that treated animals survived much longer, and showed more evidence of fibrosis, than untreated controls. Conflicting results were obtained by other workers, and Selter, Mayer, Pekanovich, Eggers and many others, as the results of experiments on animals and patients, came to the conclusion, that the various salts of copper were of no value in the treatment of Tuberculosis.

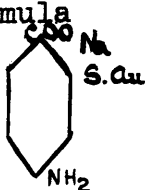
The foundation of gold-therapy in the treatment of Tuberculosis was made by Koch in 1890 when he reported that gold potassium cyanide in dilutions of 1: 1,000,000 prevented the growth of tubercle bacilli in culture. Von Behring (7) found that the presence of blood serum increased the growth preventing concentration to 1: 25,000.

Following Koch's statement Brück and Gluck (8) were the first to attempt the gold therapy of Tuberculosis in the human subject. They claimed favourable results with the application of gold potassium cyanide on external Tuberculosis, especially in combination with injections of tuberculin. The efficacy of the gold tuberculin treatment was confirmed by Bettmann (9) but in his opinion the effect was due to tuberculin; the gold merely acting as a capillary poison, causing them to dilate, thus conducting the tuberculin into the tuberculous tissue. Mayer (10) reported good results in general tuberculosis especially if the gold salt was combined with some substance like broncholin, which is said to dissolve the fatty sheath of the tubercle bacillus. Later workers denied the beneficial effects of gold potassium cyanide, and eventually the treatment was abandoned. Dixon (11) sums up the general results of this form of treatment as follows; "Results from the administration of gold salts were not better than those given by copper, whether on cultures of tubercle bacilli, or on tuberculous animals, or on patients".

The next gold preparation to be employed in the treatment of Tuberculosis was introduced by Adolf Feldt under the name of Aurocanthan. Feldt believed that the toxicity of the previous gold compounds was due to the cyanide, and to reduce this toxicity, he utilised cantharidin as a carrier for the cyanide; cantharidin having previously been shown to have an affinity for tuberculous tissue. In order to minimise the toxicity of cantharidin, he combined it with ethyldiamine; the final preparation, Aurocanthan, therefore, was a cantharidin - ethylene diaminoaurocyanide. This

preparation was soon found to be too toxic for use and as Moellgaard says (12) "This stuff has no influence on tuberculosis, it is only poisonous to the organism, which was to be expected from its chemical composition".

Feldt, in collaboration with Spies, introduced another gold salt, known commercially as Krysolgan. These workers decided from the clinical results with gold potassium cyanide and aurocanthan, that it was necessary to eliminate the cyanide from all gold compounds in chemotherapy. Accordingly they built up a water soluble sodium salt of a complex organic acid, which contained monovalent gold fixed to a benzole nucleus, having the formula



This compound Feldt called Krysolgan; it is the sodium gold salt of an aromatic amino-acid, in combination with Sulphur. This substance was made to conform with Ehrlich's principle that heavy metals have their toxicity diminished when combined with aromatic amino acids.

Feldt claims for Krysolgan, that it is not decomposed in the blood, that it has no great toxicity to the organism, and that it prevents the growth of tubercle bacilli in a concentration of 1:1,000,000. He maintains that Krysolgan has a specific action on tuberculous tissue in doses as small as .0001 gm, and that it acts as a catalyst, stimulating autolysis of the tubercles; any action on the tubercle bacilli being secondary.

Animal experiments with Krysolgan were not very promising, and in 1923 Feldt published a monograph giving the clinical results of treatment up to that date.

Good results appear to have been obtained at the beginning, where larger doses were employed, but the late results with smaller doses, as Moellgaard says (13) "only show the well known fact, that tuberculosis is a very variable disease not only in pathological development, but also in prognosis and clinical symptoms".

Comparatively recently, Feldt introduced another synthetic gold preparation which is known commercially as Solganol; it is an alkaline salt of a complex acid of gold, the gold content being 36.5%. It is claimed that the toxicity of Solganol is ten times less than Krysolgan, and so it is possible to introduce larger quantities of gold into the system.

G. Hacker (14) has published the results of Solganol treatment in sixty cases. He concludes that the substance is well tolerated, giving good results not only in the exudative type of case, but also in the mixed exudative - fibrotic forms.

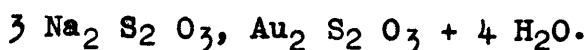
The gold preparation which has attracted most attention within recent years was synthesised by Moellgaard and introduced by him under the name of Sanocrysin in 1924.

The present thesis deals with the clinical results of treatment of a series of cases of Pulmonary Tuberculosis with this preparation.

### Section III.

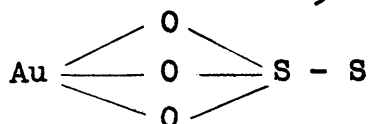
#### Sanocrysin Composition and physico-chemical properties.

The gold preparation now known as Sanocrysin was first obtained by Fordos and Gelis in 1845 (1) who considered it to be a double thiosulphate of gold and sodium, having the formula

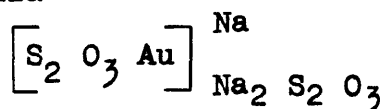


Vanino, in the handbook of Gmelin Krant 1914 (2) gives a description of the same compound as 'Natriumaurothiosulphate' and ascribes to it properties similar to that of Fordos and Gelis.

Moellgaard (3), as the results of his analysis, concludes, that the body  $\text{Au} (\text{S}_2 \text{ O}_3) \text{ Na}_3$  can be built up only by using trivalent gold ; that the Au is fixed to the oxygen as  $\text{Au}^{+++}$ , and not to Sulphur as  $\text{Au}^+$ ; that the complex ion  $\text{Au S}_2 \text{ O}_3$  has the formula,



and that the whole gold compound known as Sanocrysin has the formula



We can conclude from determinations of the electrical conductivity, and the depression of the freezing point of Sanocrysin, that the substance is dissociated in such a way, that the therapeutic agent of the compound is the negatively charged ion  $\text{Au O}_3 \text{ S}_2$ .

The physico-chemical properties of Sanocrysin according to Moellgaard are as follows :-

- (1) Easily soluble in water but non hygroscopic
- (2) Aqueous solution is almost neutral.
- (3) Diffusion velocity is about 75% of the diffusion velocity of iodine under similar conditions.

- (4) Dilute mineral acids do not affect the salt at ordinary temperature, but when heated with strong nitric or hydrochloric acid, it decomposes, and liberates its gold. Diluted aqueous solutions stand sterilizing at  $130^{\circ}\text{C}$  without decomposition. 1% - 5% solutions are clear for about 14 days when kept in a dark room, and in daylight they decompose slowly, forming a brown precipitate of  $\text{Au}_2\text{S}_2$ .
- (5) The dry salt is very stable, but a small quantity of water makes it decompose slightly, in three to four weeks, giving the salt a yellow colour.
- (6) Sanocrysin does not precipitate protein, and a solution of 1% in serum can be heated up to  $40^{\circ}\text{C}$  for 24 hours, without forming any precipitate, or producing any blackening of the fluid.
- (7) When oxidised with  $\text{H}_2\text{O}_2$  in alkaline solution, Sanocrysin is decomposed quantitatively into metallic gold and sodium sulphate.

## Section IV.

### Experimental work with Sanocrysin.

Moellgaard maintains, that in sanocrysin, he has found a suitable chemotherapeutic agent for the treatment of tuberculosis, viz.,

1. It is easily soluble in water, and rapidly diffusible, due to the small size of the molecule.
2. It is slowly eliminated by the organism.
3. It does not decompose in the body, with the formation of poisonous substances.

Moellgaard's next endeavour was to prove, experimentally, the bactericidal action of sanocrysin on the tubercle bacillus. He conducted three series of experiments.

1. Researches into the influence of sanocrysin on the tubercle bacillus in culture. The results of this work indicate, that sanocrysin, in concentration of 1: 100,000, prevents the growth of the bacilli in culture, and that a concentration of 1:1,000,000 exerts some inhibitory influence.
2. Researches into the influence of sanocrysin, on the morphological and staining characteristics of the tubercle bacillus. In his book, 'Chemotherapy of Tuberculosis', he illustrates the results of his investigations, by means of microphotographs. Bacilli, treated with 1% sanocrysin, and then stained, are shown to have lost their acid fastness, some are gold blackened, and many have become granular. He also shows, that, if the sanocrysin-treated bacilli, after being decolourized with  $\text{H}_2 \text{S O}_4$ , are treated with a 1% solution of  $\text{Na}_2 \text{C O}_3$ , the majority of them regain their red colour. From these experiments,

Moellgaard concludes that "sanocrysin under certain conditions makes the fatty colloid system, which protects the bacilli, penetrable to hydrogen ions, and the blackening of the bacilli shows that the gold containing ion of the sanocrysin is travelling into their bodies. The granulation and curling of the bacilli show that it affects their morphology very seriously". (1) He also found that various cultures have a different resistance to sanocrysin.

3. Researches into the ability of sanocrysin to prevent artificially infected guinea pigs from developing generalized tuberculosis. All the control animals, five in number, developed generalized tuberculosis, while four, out of the five treated animals, escaped.

Before attempting curative experiments on animals, Moellgaard investigated the effects of the drug on normal, non-tuberculous animals, mainly employing calves. He found, that sanocrysin, in doses of 2 centigrammes per kilo of body weight, has no injurious effect on the blood, heart, blood pressure, body temperature, or liver. Occasionally, when this dose was employed at short intervals, slight albuminuria occurred, but disappeared after three or four days, the kidneys soon accustoming themselves to larger doses. He also found, that very large doses may produce diarrhoea, but doses less than 3 centigrammes per kilo. of body weight have no irritating effect on the intestines, when pure sanocrysin is used.

On investigating the excretion of gold, Moellgaard found that sanocrysin is excreted principally through the kidneys, and only to a very small extent through the intestinal canal. He discovered gold in the urine, four to six days after intravenous injection of 1 gm. of



sanocrysin, thus proving a cumulative action, and augmenting the possibility of the substance diffusing into tuberculous tissue.

Moellgaard next determined the results of intravenous injections of sanocrysin in tuberculous animals. He found that the injections are followed by an acute intoxication, characterized by, albuminuria, myocarditis, oedema of the lungs, and a fall in temperature, which is accompanied by shock. He attributes this shock reaction to the liberation of toxic substances from the tuberculous foci, and he claims that it is analagous to 'tuberculin shock'. He claims that sanocrysin is bactericidal, and on the disintegration of the tubercle bacilli, toxic substances are liberated. He studied the phenomena of shock in calves, and found that this reaction could be cured and prevented, by the intravenous injection of a sufficient dose of a specific serum. The serum is prepared by the injection of dead tubercle bacilli and tuberculin, into calves, which give a negative tuberculin test.

Moellgaard found, on continued investigation, that serum treated animals, and animals immune from shock, react to sanocrysin, with rise of temperature, slight albuminuria, exanthematous skin eruptions, mild diarrhoea, and loss of weight. He discovered that the animal loses these reactions as the cure advances, and when the animal is clinically cured, no reactions occur. He maintains that the reactions result from the liberation of toxins from the destroyed bacilli, and not to the sanocrysin per se. To strengthen his argument, he cites the cases of two calves, in whom an abscess had formed around the veins in the neck, where the bacilli were injected. (2) The animals were treated with sanocrysin, and after a time

they were free from reactions, and appeared to be fully cured. One gramme of sanocrysin was injected into the abscesses, and both calves showed violent reactions, one with haematuria, and the other with a marked rise of temperature. Moellgaard explains this as follows (3)

"This means that the disease outside the abscess has been reduced nearly to sterilization, but the bacilli in the abscess have been protected by its thick fibrous wall, poor of vessels. When the sanocrysin, however, was injected direct into the abscess, the bacilli were dissolved, and the reactions appeared again".

The following are the main points from Moellgaard's conclusions with his curative experiments on animals.

1. Sanocrysin in large doses, combined with serum treatment, saves the lives, and clinically heals, animals affected with grave miliary, and pneumonic tuberculosis.
2. Complete sterilization is very difficult, and depends on the extent of caseous destruction. In mild cases, with little tissue destruction, complete sterilization occurs, but in the more advanced cases, where large numbers of tubercles are present, even although calcified, tubercle bacilli can be found by the guinea pig test.
3. Small doses produce an improvement in cases with chronic developing disease.
4. In acute cases with grave infection, small doses retard the development of the disease when treatment commences shortly after infection. When these doses are employed on fully developed pneumonia, they have no curative effect, but rather an accelerating influence, due to large focal reactions.

5. In advanced disease, where the infecting bacilli are very virulent, cure cannot be effected, owing to the inability of the immune serum to combat the profound toxæmia.

From his animal experiments, Moellgaard maintains that he has indirect evidence, that sanocrysin has a specific bactericidal action on the tubercle bacillus, and that the organism is destroyed in vivo, with the liberation of toxin.

Bang (4) in 1925, as the result of animal experiments with a gold salt, sodium aurothiosulphate, which resembled sanocrysin, attacked Moellgaard's position. His main points are :-

1. Sanocrysin in concentration of 1:3,200 does not inhibit the growth of tubercle bacilli in culture.
2. It has no curative power on experimental tuberculosis in rabbits.
3. Moellgaard's antitoxic serum cannot be specific, because it is incapable of protecting guinea pigs against genuine tuberculin shock, provoked by the smallest lethal dose of tuberculin.

Moellgaard (5) replied to Bang, that the sodium aurothiosulphate, used in his experiments, may differ essentially from "Moellgaard's sanocrysin"; that sanocrysin may be a real bactericide in vivo, even if its action is variable in vitro, and that sanocrysin may fail to cure tuberculosis in rabbits, and still be effective in other mammals.

Sir Almroth Wright (6) found that sanocrysin, in dilutions of 1 in 250, is without effect on tubercle bacilli in blood. Moellgaard has admitted recently, that the nature of culture and medium has an important influence on the inhibitory power of sanocrysin, the

lowest growth-preventing concentration being found in a culture taken directly from the sputum, and the highest in old laboratory cultures.

According to the British Medical Research Council's first report on sanocrysin, Moellgaard's antitoxic serum has no accreditable function, and Cummings states that the serum is incapable of preventing the shock which may follow the injection of tuberculin into a tuberculous rabbit.

Madsen and Mörch ( 7 ) published their results of sanocrysin treatment of experimental tuberculosis in rabbits. They employed two different cultures for infecting the animals, an attenuated and a virulent. They show that in animals infected with the former, it is possible to heal the disease with gradually increasing doses of sanocrysin, while in animals infected with the latter, large doses have to be employed to arrest the disease. They also found that sanocrysin treatment, commencing with the infecting dose, fails to have a curative effect.

The above workers published the results of further animal experiments in 1928 ( 8 ). They found a smaller proportion of cures in this series of experiments, and attribute it to loss in virulence of the culture, which was the same, as that employed in the previous experiments. They also bring forward the fact, that, when treatment was commenced 3 to 5 days after the infecting dose, all the animals survived.

The recent report by the Sanocrysin Research Committee of Japan ( 9 ) deals a severe blow to Moellgaard's work. The main points from their experimental work in vitro, and in animals are,

1. Sanocrysin inhibits the growth of tubercle bacilli in

concentration of 1:10,000.

2. Sanocrysin in .1% to 1% solutions does not injure the pathogenicity of the tubercle bacillus.
3. Moellgaard's antitoxic serum does not suppress albuminuria, and does not prevent shock.
4. Curative experiments with rabbits and guinea pigs give no conclusive results.
5. There is no evidence of a curative influence of sanocrysin in calves infected with tuberculosis.
6. Sanocrysin has no specific bactericidal action on tuberculosis.

The present position, with regard to experimental work with sanocrysin, appears to be conflicting. The excellent results, obtained by Moellgaard in his early experiments, have not been repeated, although the work of Madsen and Mörch appears hopeful. The results from the Japanese workers are decidedly negative. The difficulty of the interpretation of the results of sanocrysin treatment in animals is enhanced by the consideration of the dosage employed, the nature of the culture, and the resistance of the animal. A similar position arose in the early work on the salvarsan treatment of syphilis, and it was only by the results of numerous experiments that the salt became established as a specific for this disease.

The following relevant facts appear from the results of experimental investigations up to the present time.

1. Sanocrysin, even if not bactericidal, exerts some inhibitory influence on the tubercle bacillus.
2. In tuberculous animals, sanocrysin has the most curative effect, when the infecting strain is virulent, i.e. in cases with little fibrous tissue reaction, and with a good blood supply round the foci, thus facilitating the action of the salt on the bacilli.

## Section V.

### The clinical results in the treatment of 22 cases of pulmonary tuberculosis with sanocrysin.

#### (a) Types of cases.

The cases chosen in the present investigation were those, which had not responded to the ordinary sanatorium measures of rest and graduated exercise.

Early cases, where rest, good nutrition, and climatic environment would achieve a satisfactory result, were considered unsuitable for sanocrysin. Gastro-intestinal disturbance and impairment of kidney function were considered contra indications, on account of those conditions being aggravated by the metallic excretion.

The cases chosen may be divided into four groups, viz:-

Group 1. Cases with early lung infiltration and scanty physical and radiological evidence of disease. Four cases were chosen in this group, three of whom had had sanatorium treatment for a considerable time, and their condition still remained unsatisfactory, the temperature remaining febrile, and exercise being badly tolerated.

Case numbers of the group = 15, 17, 18 and 19.

Group 2. Cases in whom the tuberculous process had involved more than one lobe of the lungs, accompanied by considerable systemic disturbance. Fourteen cases are included in this group, all of whom had sanatorium treatment for some time, before sanocrysin was commenced.

Case numbers of group = 1 to 14

Group 3. Cases with advanced and active tuberculosis. Three cases were chosen in this group.

Case numbers of the group = 20 to 22

Group 4. One case with an incomplete artificial pneumothorax on one side, and active tuberculous disease in the other.

Case number = 16

All the cases under review, have been classified according to the classification employed by Crockett.(1)

The scheme is a modification of the Turban-Gerhardt classification, and the symbols L and S are employed. L, indicates the amount of lung tissue involved, and is accordingly graded into  $L_1$ ,  $L_2$ , and  $L_3$ . S, indicates systemic disturbance and is graded into  $S_1$ ,  $S_2$  and  $S_3$ .

If the sputum is positive for tubercle bacilli, the number present is represented by +, ++, and +++. No sputum is indicated by 0. An advanced case of pulmonary tuberculosis with wasting, rapid pulse, and remittent temperature, will be classified  $L_3 S_3$  +++.

On considering the aforementioned groups, it is found that the majority of cases in each group come under a common classification, viz:-

Group 1 =  $L_1 S_2$ ., Group 2 =  $L_2 S_2$ ., Groups 3 & 4 =  $L_3 S_3$ ..

According to the continental classification, the cases under review are considered exudative or fibro-exudative.

## (b) Administration and dosage.

In the present series of cases, sanocrysin was injected intravenously in a concentration of 1 in 20 in sterile distilled water.

The original scheme of dosage, established by Secher and Wurtzer (2), was based on the results of Moellgaard's animal experiments.

The following table outlines their scheme:

## Body weight

Kilograms.	1st day	4th day	12th day	20th day	28th day
80 and more	·5	1	1	1	1
70	·5	·75	1	1	1
60	·5	·5	·75	1	1
50	·5	·5	·5	·75	·75
40	·25	·5	·5	·5	·5
30	·25	·25	·25	·5	·5
20	·25	·25	·25	·25	·25

As a rule, therefore, the initial dose in an adult is ·5 gms. These workers consider this a trial dose, and hope to excite a focal reaction, with considerable rise of temperature. Their object is to produce an intensive concentration of sanocrysin in the organism, in order to exert a bactericidal effect on the tubercle bacilli. They do not aim at producing focal reactions, to stimulate the formation of connective tissue, but they desire to eliminate the tubercle bacilli, before healing of the affected tissues take place.

The more recent work of other investigators favours a more lenient dosage. They maintain that the modified dosage has not detracted from the ultimate results, and precludes the danger of provoking uncontrollable focal reactions.

Faber (3) describes a method of dosage, whereby the possibility of shock is eliminated, and the use of serum



When a reaction occurred, viz., gastro-intestinal disturbance, albuminuria, stomatitis, rash, or severe temperature reaction, the dose of the subsequent injection was not increased, and it was not given until the reaction had completely passed off.

The total amount of sanocrysin given in the course was 6 - 8 gms. A second course of treatment was given to 13 patients at an interval of two months after the initial course. In the second course the dosage was rapidly increased, to the maximum, at weekly intervals.

The maximum dose was repeated till no further reaction occurred.

(c) Control and Supervision of treatment.

As a routine measure, during the 1st course of sanocrysin treatment, all patients were kept in bed. During the 2nd course, they were kept in bed, only on the day of injection.

The urine was tested daily for albumen.

In attempting to assess the progress of the patient's condition under treatment, the following criteria were observed:-

1. A weekly record of weight was kept.
2. The sputum was measured daily, and a bacteriological examination was made at regular intervals. If tubercle bacilli were absent, the antiformin concentration method was employed.

In the following analysis of cases, a chart is appended to each case, showing the weekly amount of sputum, and the results of bacteriological examination.

3. A routine physical examination was made at monthly intervals.
4. A radiogram was taken before and after treatment.
5. Red cell sedimentation rates, and polynuclear counts, were recorded, before, during, and after treatment.

It is necessary at this stage to evaluate the significance of the above blood controls employed in this investigation.

Fahreus ( 8 ) has shown, that sedimentation of red cells, is due to the action of haemagglutinins, the red cells when agglutinated, dropping down. He also found, in cases where the sedimentation rate was rapid, that the most important change in the blood plasma, was an increase of fibrinogen and serum globulin. Beaumont and Dodds( 9 ) point out, that the destruction of tissue proteins results in an increase in the fibrinogen and serum globulin content of the blood.

Westergren (10) and Clegg (11) found that there is little physiological variation in the rate of sedimentation of red cells, but Heaf (12) Cutler, (13) and Greisheimer (14) found that the rate is slightly increased in women.

In pulmonary tuberculosis, these observers conclude that the sedimentation rate, when considered in relation to clinical observations, is a guide to the activity of the lesion. They also consider that the sedimentation rate is more useful in prognosis, than in diagnosis. Cummings and Acland (15) think that the sedimentation rate should be of great utility in the study of new methods of treatment of tuberculosis.

It has been generally found, that the sedimentation rate of red cells increases in proportion to the extent, and activity of the lesion. Wingfield and Goodman (16) state that the graph of the sedimentation rate, in a normal individual, appears as a straight line, while that of an abnormal condition appears as a curved line, the maximum fall taking place in the first two hours. This is in agreement with the present writer's observations, and in the present series of cases, the rate at the end of the 1st hour was considered the most important. In the present investigation, the technique employed was Westergren's modification of the Fahreus method. It consists in taking .4 c.cs of 3.8% solution of sodium citrate into a syringe, and filling the syringe to the 2 c.c. mark, with blood from the patient's vein. The blood is thoroughly mixed with the citrate, and transferred to a test tube. The blood is then sucked up to the zero mark in a special pipette, which is placed vertically in a rack. The pipette is 30 cms. long, has an internal diameter of 2.5 mm., and is divided into 200 equal divisions. Readings are taken at end of 1, 2, and 4 hours.

Westergren, as the result of observations on patients, suffering from pulmonary tuberculosis, came to the

following conclusions, regarding the readings of the sedimentation rate at the end of 1 hour.

1. A fall of 3 m.m. is normal.
2. " " " 4-6 m.m. is doubtful.
3. " " " 7-12 m.m. is probably pathological.
4. " " " over 12 m.m. is certainly pathological.

In the present series of cases, the sedimentation rate was taken at the end of the 1st, 2nd and 4th hours, but in several cases at the commencement of treatment, only the 1st hour readings were taken. The results have been recorded graphically, and in the analysis of cases, a graph is appended to each case.

The following graph (fig.1) a modification of that suggested by Davies, (17) shows the classification of curves.

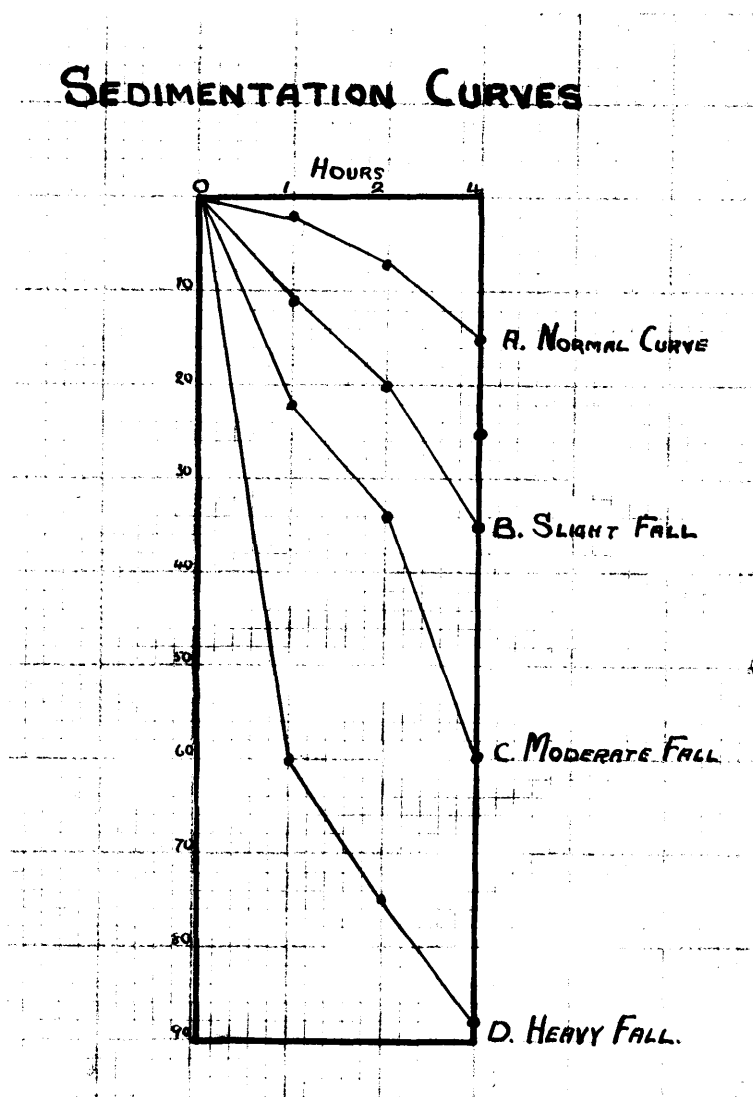


Figure 1.

The other blood control employed in this investigation was the polynuclear count, i.e., the modification of the Arneth count as introduced by W.E.Cooke in 1914.

The technique consists in staining a blood film with Giemsa's stain, and dividing the polymorphic leucocytes into five classes, according to the number of lobes in each nucleus. Thus, a nucleus with one lobe belongs to Class I, with two lobes to Class II, etc. The cells in Class I, are the young leucocytes, newly liberated from the marrow, and as they grow older, they gradually progress to the higher classes, where they die out. Class V, contains the oldest cells which are on the verge of death.

The count is written as percentages of cells in the various classes.

The normal count, in the healthy individual, according to Cooke and Ponder ( 18 ) is

I	II	III	IV	V
10	25	47	16	2

This is represented graphically as in fig. 2.

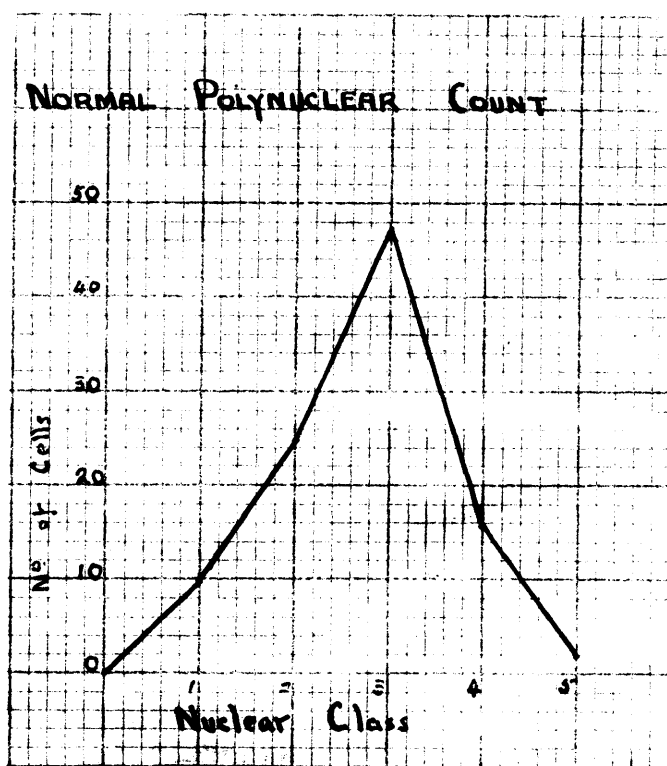


Figure 2.

The weighted mean is a sensitive measure of the state of the count. It is arrived at by multiplying the number of cells in each class, by the number of the class, estimating the total, and dividing by 100.

Thus the weighted mean of the above count is 2.73.

Cooke and Ponder maintain that "an excellent criterion of normality is that the weighted mean of a count shall not be less than 2.4, although a rougher and less reliable guide of less than 40 cells in the first two classes may be substituted". (19).

In all disease conditions associated with toxæmia, the curve of the polynuclear count is displaced to the left, and the degree of displacement is an index of the toxæmia. This phenomenon is due to the toxin stimulating marrow production, with the resulting increase of leucocytes belonging to Class I and II in the blood stream. A displacement of the curve occurs in pulmonary tuberculosis; the unfavourable case shows an increasing left hand drift, and the improving case shows a gradual return to the normal. Cooke and Ponder observe that "in estimating the results of treatment the count is invaluable, and the time has come when it should be used as a criterion of cure". (20).

In the present series of cases, the polynuclear counts were estimated in each case, at intervals during treatment, and the results have been recorded graphically.

In the analysis of cases, the graphs of each case are appended.

(d) Analysis of cases.

In the following analysis of cases, note that the charts and figures are placed on the page facing the notes on the cases.

The following explanatory notes are necessary in connection with the controls.

1. In the graphs of the sedimentation rates, the 1st courses are drawn in black ink and the 2nd courses in in red ink. The graphs at the commencement and during treatment are indicated by dotted lines, while those at the end of 1st and 2nd courses are indicated by continuous lines.
2. The curves of the polynuclear counts are drawn in different coloured inks. An index of the weighted means is given alongside each figure.
3. The sputum charts and radiograms are self explanatory.

## Case 1.

Ernest Martin, age 21 years.

Commenced Sanocrysin. 1st course 19.4.28. Completed 4.7.28.

" " 2nd " 11.10.28. " 19.11.28.

Duration of disease:- 2 years.

Symptoms:- Cough and spit, loss of weight, pains in chest, and slight dyspnoea on exertion.

Had sanatorium treatment for 20 weeks, and condition remained unsatisfactory before sanocrysin commenced.

Sputum:- T.B.+++.

Average diurnal temperature:- 97.6 - 99.2.

" " pulse rate :- 80 - 90.

Physical signs in chest:- P.N. markedly impaired over left upper lobe and slightly impaired over right upper lobe. B.S. weak, jerky, and granular on both sides, with Exp.+ and V.R.+ at the left subclavicular region.

Radiogram:- (fig. 3).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:-

1st course = .05, .1, .2, .25, .35, .5, .6, .75, 1, .85, 1, 1 = 7.15 gms.

2nd " = .1, .25, .5, .75, .75, 1, 1 = 4.35 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.2.
2. " " pulse rate :- 72 - 84.
3. Exercise:- On full sanatorium régime.
4. Weight:- Gained 7 lbs.
5. Sputum:- See chart 1. Note. Sputum quickly cleared up.
6. Radiological:- (figs. 3 & 4).

Note the partial resolution of pneumonic area on left side, the disappearance of fuzziness from the infiltrative nodules in both upper lobes, and the general increase of fibrosis.



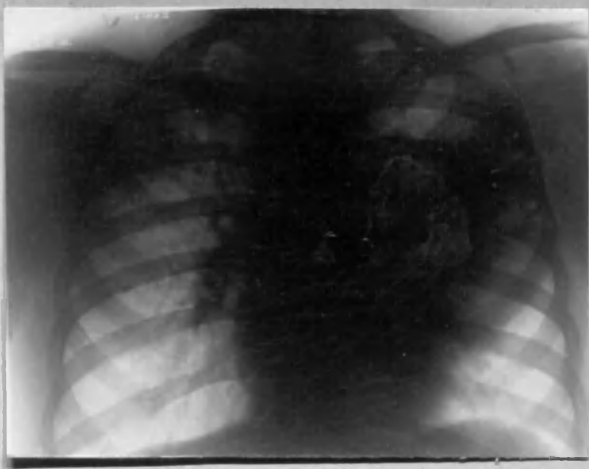


Fig. 3. Before treatment.

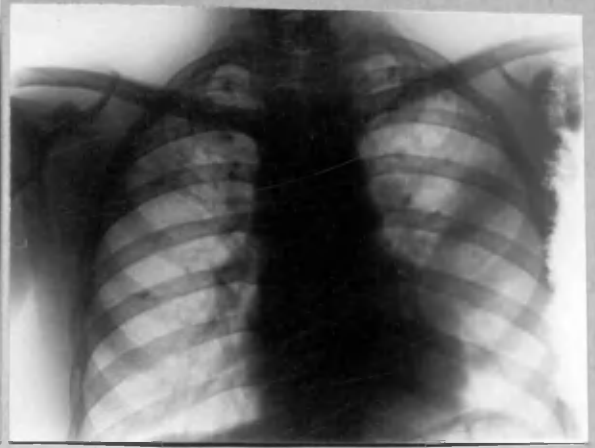


Fig. 4. After treatment.

Fig. 3 shows a pneumonic area in left side, and considerable active disease in right upper lobe. Fig. 4 demonstrates the resolution of pneumonic area in left side and the clearing of exudative processes in right side.

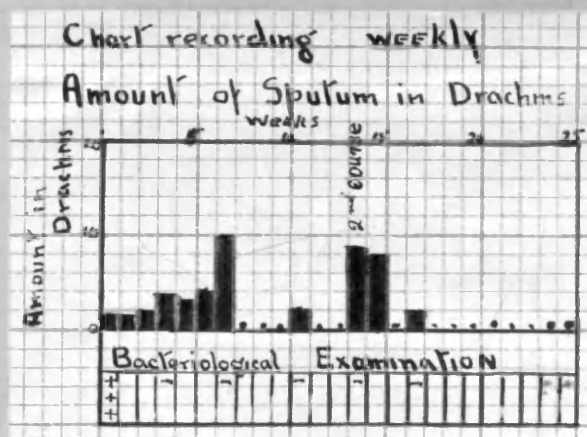
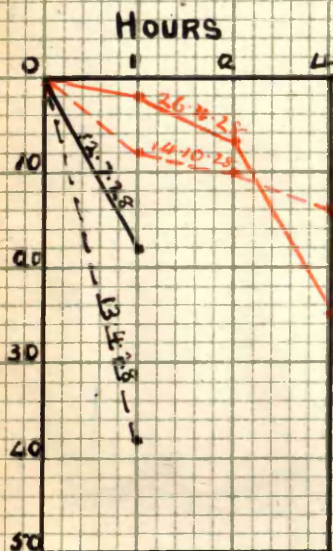


Chart 1.

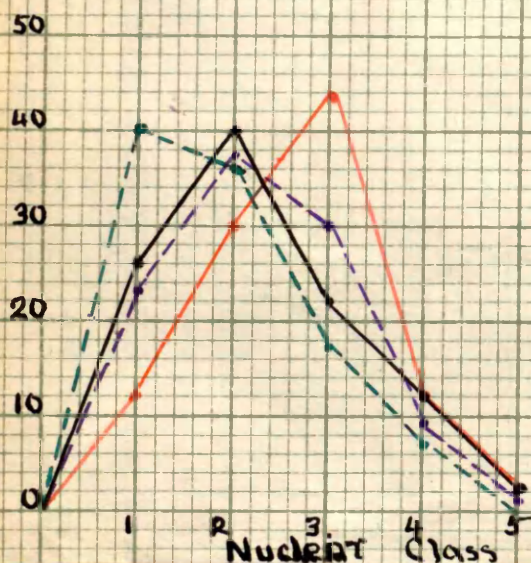
# SEDIMENTATION RATE



---- During 1<sup>st</sup> COURSE  
 ——— END of 1<sup>st</sup> COURSE  
 ---- During 2<sup>nd</sup> COURSE  
 ——— END of 2<sup>nd</sup> COURSE

Fig. 5

# POLYNUCLEAR COUNT



——— 25.8.28 W.M. 2.21  
 ---- 14.10.28 W.M. 1.71  
 ---- 26.11.28 W.M. 2.28  
 ——— 12.2.29 W.M. 2.78

Fig. 6.

7. Physical signs:- P.N. slightly impaired over both upper lobes. B.S. harsh and no adventitious sounds audible. The prolonged expiration has gone from left subclavicular region.

8. Red cell sedimentation rate:- (fig. 5).

Note the decrease of fall in 1st hour after both courses.

The improvement is continuous and maintained.

9. Polynuclear count:- (fig. 6).

Note the gradual swinging of the curve towards the right; a normal weighted mean is obtained at the completion of second course.

Reactions to sanocrysin:- (1) Focal (2) Slight albuminuria, lasting a few days after large doses.

#### Resume

The patient markedly improved as evidenced by the radiograms, physical signs, and capacity for exercise. The polynuclear count shows a reduction of toxaemia and the sedimentation rate indicates a favourable prognosis.

The patient's condition was maintained three months after discharge.

Classified result:- Markedly improved.



## Case 2.

Ernest Withers Age 30 years.

Commenced Sanocrysin. 1st course 3.6.28 Completed 6.9.28.

" " 2nd " 22.11.28 " 31.12.28.

Duration of disease:- 1 year.

Symptoms:- Persistent cough and spit, night sweats, loss of weight, and dyspnoea on exertion.

Sputum:- T.B.+

Average diurnal temperature:- 97.2 - 98.6.

" " pulse rate :- 88 - 92

Physical signs in chest:- Right side. P.N. impaired over upper and middle lobes. B.S. vesico bronchial in infra clavicular region. V R ++. Fine post tussive râles and distant rhonchus, audible over upper lobe.

Left side. P.N. impaired along scapular border, where fine crepitant râles are audible.

Radiogram:- (fig. 7).

Classification:- L<sub>2</sub> S<sub>1</sub> +

Sanocrysin given:-

1st course = .05, .1, .2, .2, .35, .5, .6, .75, .75, 1, 1, 1, 1 = 7.5 gms.

2nd " = .1, .25, .5, .7, 1, 1, 1, = 4.55 gms.

Results of treatment.

1. Average diurnal temperature:- 97 - 98.

2 " " pulse rate :- 84 - 88.

3. Exercise:- Full sanatorium régime.

4. Weight:- Gained 3 lbs.

5. Sputum:- see chart. 2.

Note. Sputum diminished after 1st course, and increased on commencement of 2nd course. This increase was due to coryza. Two months after completion of 2nd course, the sputum was very scanty. Sputum remained T.B.+

6. Radiological:- (figs. 7 & 8).

Note. the striking absorption of exudative disease in right upper and middle lobes. There is increased fibrosis in both upper lobes and a cavity is defined around right hilum.

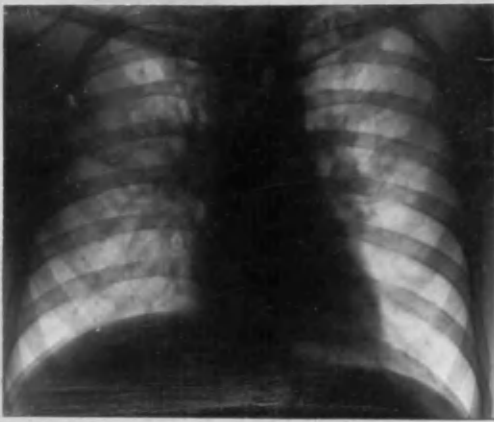


Fig. 7. Before treatment.

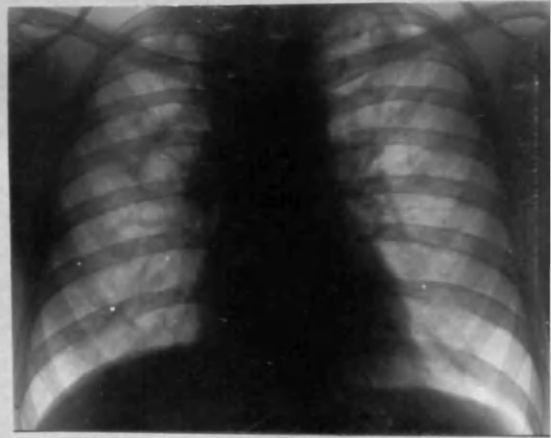


Fig. 8. After treatment

Fig. 7 shows a pneumonic area in right side and active nodulation in left upper lobe. Fig. 8 shows the striking resolution of pneumonic area, and demonstrates the fibrous outline of cavity round right hilum.

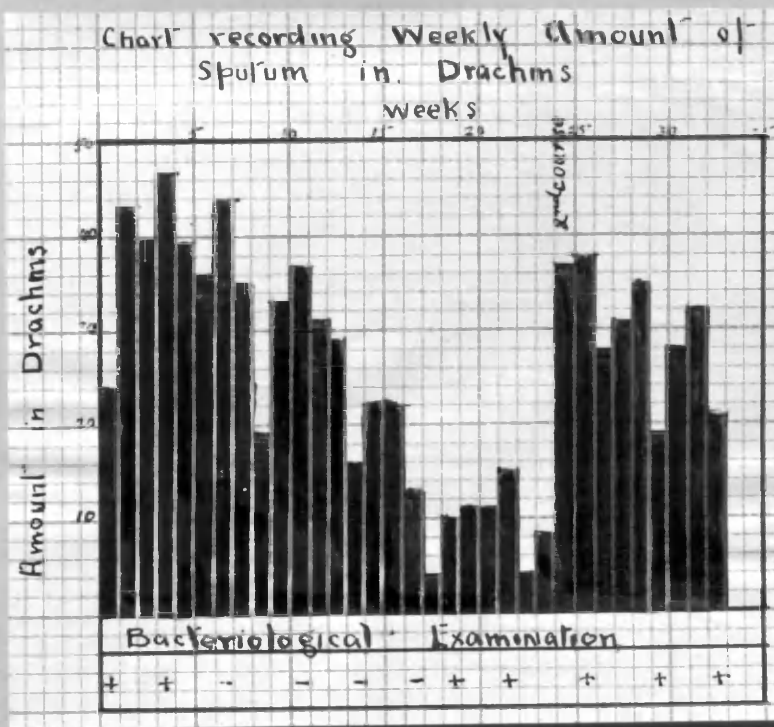


Chart 2.



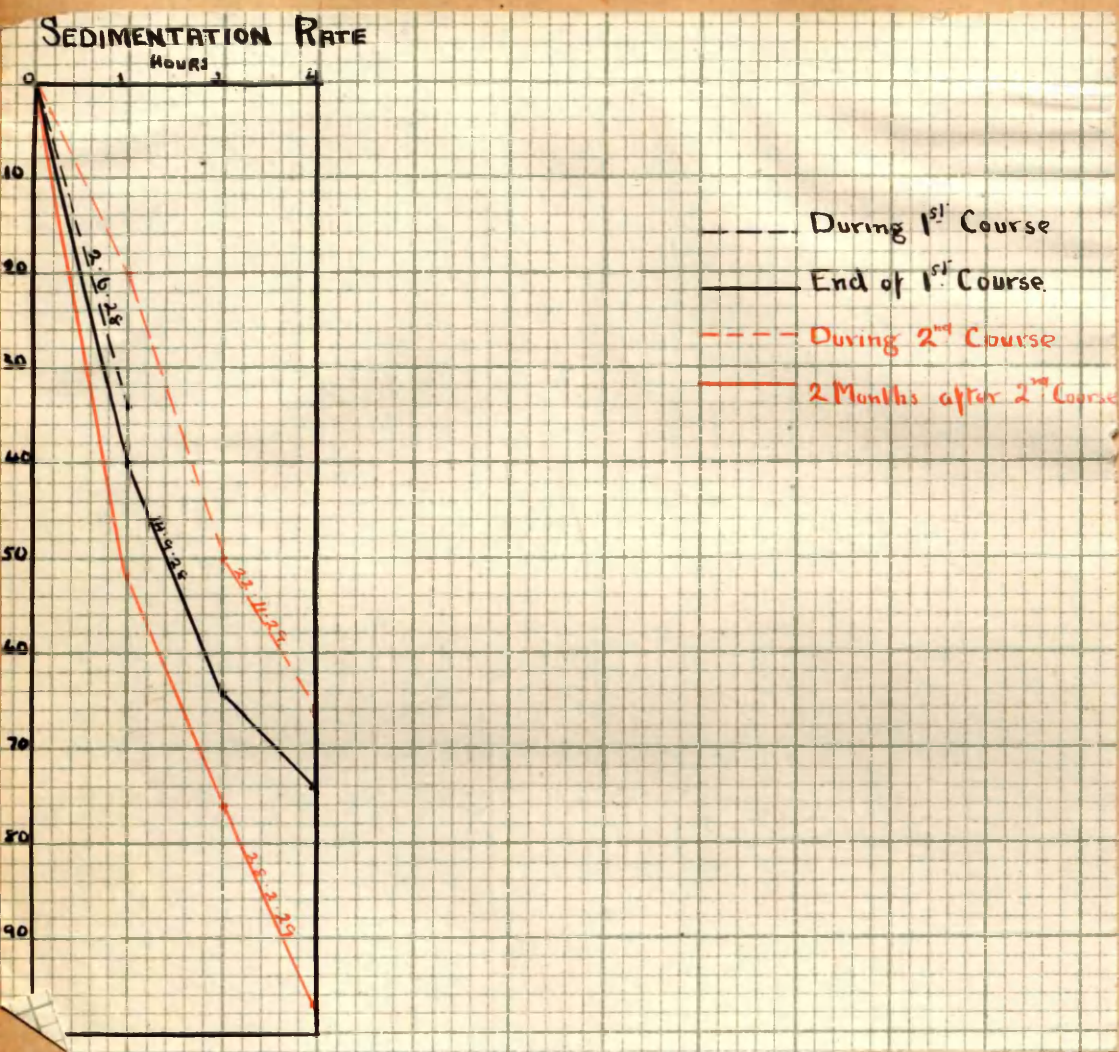


Fig. 9.

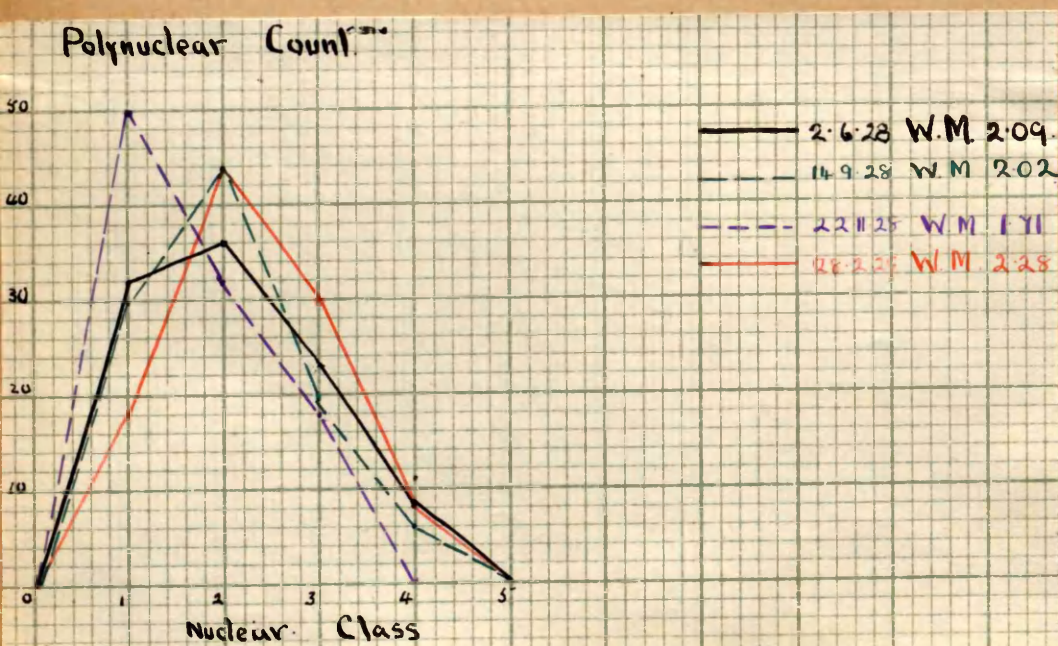


Fig. 10.

Case 3:

Lawrence Moore Age 19 years.

Commenced Sanocrysin. 1st course 27.5.28. Completed 6.9.28.

" " 2nd " 29.11.28. " 26.1.29.

Duration of disease:- 6 months.

Symptoms:- Cough and spit, loss of weight, small haemoptysis and dyspnoea on exertion.

Before sanocrysin commenced he had 14 weeks sanatorium treatment, but condition remained unsatisfactory, due to frequent bouts of active disease.

Sputum T.B.+++.

Average diurnal temperature:- 97 - 99.

" " pulse rate :- 90 - 94.

Physical signs in chest:- Right side. P.N. impaired over upper and middle lobes. B.S. vesico-bronchial in upper lobe accompanied by crepitant râles and occasional creaks. Air entry poor over lower lobe.

Left side. P.N. impaired at apex where occasional fine post-tussive râles are audible. B.S. are harsh at base.

Radiogram:- (fig.11 ).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:- 1st course = .05, .05, .1, .1, .2, .2, .2, .25, .35, .45, .5, .75, 1, 1, 1, 1 = 7.2 gms.

" " 2nd " = .25, .5, .75, 1, 1, 1, 1, 1 = 6.5 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97 - 98.2.

2. " " pulse rate :- 80 - 84.

3. Exercise:- Full sanatorium régime.

4. Weight:- Gained 10 lbs.

5. Sputum:- see chart. 3.

Note. Sputum increased at end of 1st course and diminished at end of 2nd course. It remained positive for tubercle bacilli throughout treatment.

6. Radiological:- (figs.11&12 ).

Note the absorption of 'woolly' nodules, and the definite fibrous outline of cavity, in right upper lobe, after treatment.

Case 3:

Lawrence Moore Age 19 years.

Commenced Sanocrysin. 1st course 27.5.28. Completed 6.9.28.

" " 2nd " 29.11.28. " 26.1.29.

Duration of disease:- 6 months.

Symptoms:- Cough and spit, loss of weight, small haemoptysis and dyspnoea on exertion.

Before sanocrysin commenced he had 14 weeks sanatorium treatment, but condition remained unsatisfactory, due to frequent bouts of active disease.

Sputum T.B.+++.

Average diurnal temperature:- 97 - 99.

" " pulse rate :- 90 - 94.

Physical signs in chest:- Right side. P.N. impaired over upper and middle lobes. B.S. vesico-bronchial in upper lobe accompanied by crepitant râles and occasional creaks. Air entry poor over lower lobe.

Left side. P.N. impaired at apex where occasional fine post-tussive râles are audible. B.S. are harsh at base.

Radiogram:- (fig.11 ).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:- 1st course = .05, .05, .1, .1, .2, .2, .2, .25, .35, .45, .5, .75, 1, 1, 1, 1 = 7.2 gms.

" " 2nd " = .25, .5, .75, 1, 1, 1, 1, 1 = 6.5 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97 - 98.2.

2. " " pulse rate :- 80 - 84.

3. Exercise:- Full sanatorium régime.

4. Weight:- Gained 10 lbs.

5. Sputum:- see chart. 3.

Note. Sputum increased at end of 1st course and diminished at end of 2nd course. It remained positive for tubercle bacilli throughout treatment.

6. Radiological:- (figs.11&12 ).

Note the absorption of 'woolly' nodules, and the definite fibrous outline of cavity, in right upper lobe, after treatment.



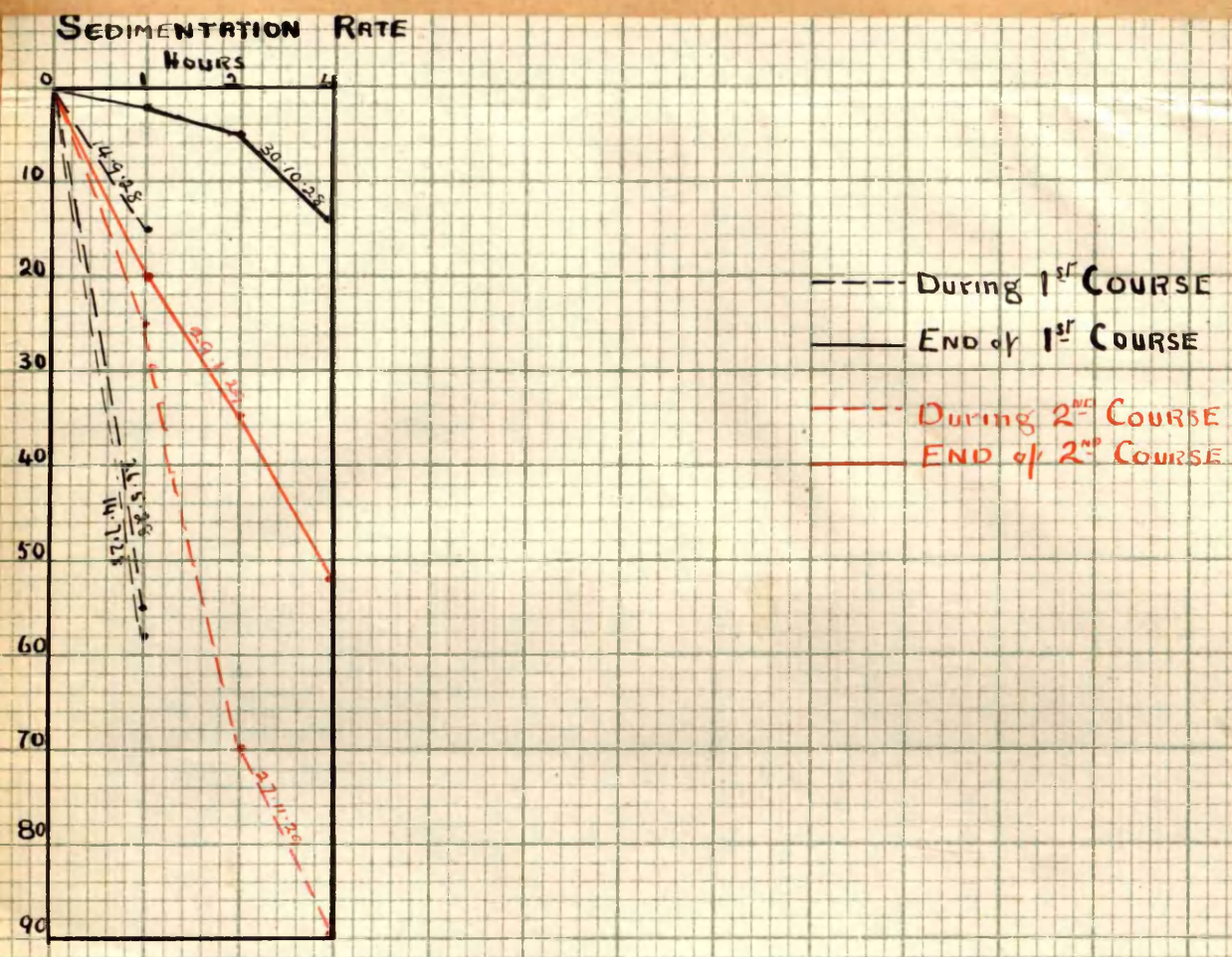


Fig. 13.

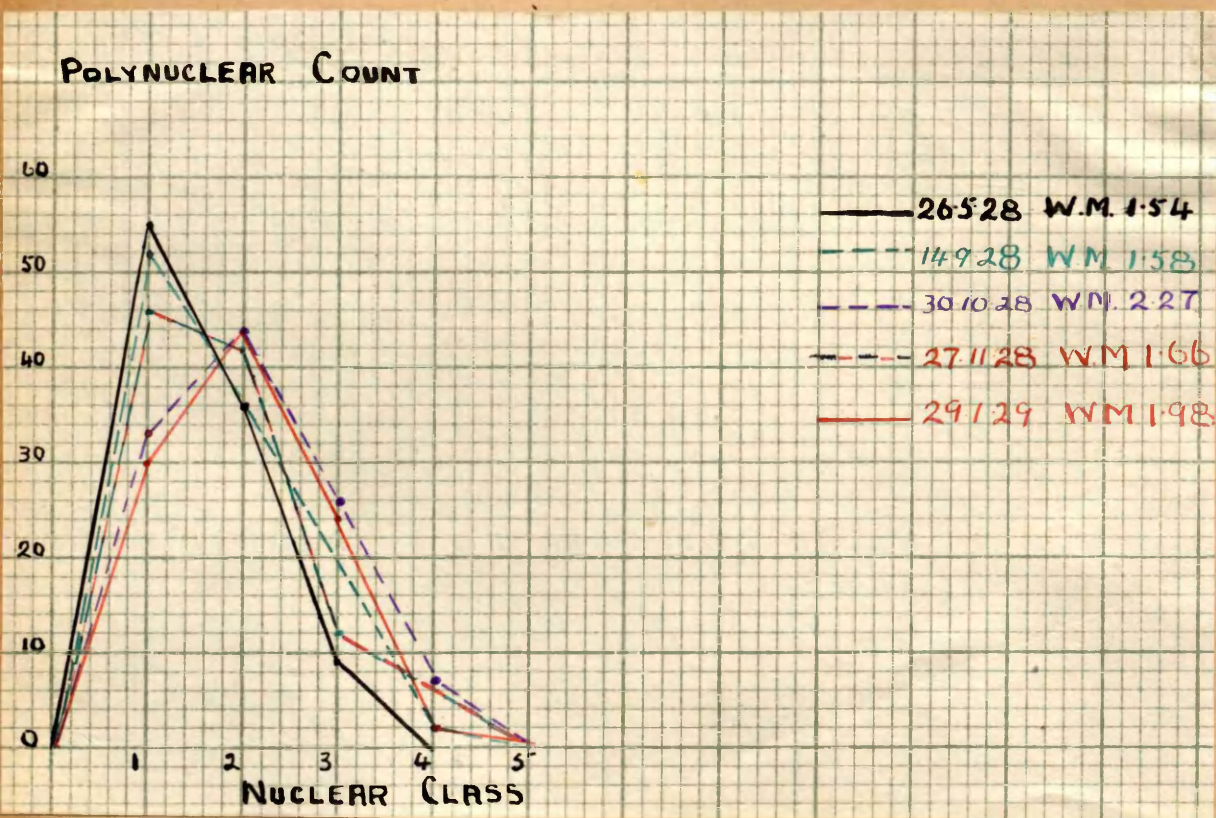


Fig. 14.

7. Physical signs:- Right side. P.N. impaired over upper lobe where broncho vesicular B.S. and squeaking rhonchus are present.

Left side. P.N. impaired over apical region and expiration is prolonged.

8. Red cell sedimentation rate:- (fig. 13).

Note the steep initial fall, the marked improvement at the end of 1st course, and the falling away at the end of 2nd course.

9. Polynuclear count:- (fig. 14).

Note the gradual improvement in the curves while he is under treatment. The optimum curve is obtained at the end of 1st course. The curve has improved from the beginning to the end of 2nd course.

Reactions to sanocrysin:- Focal.

#### Resume.

This patient shows a marked improvement in the radiological and physical signs on the completion of treatment. On readmission for 2nd course, the improvement was not maintained, as evidenced by the increase in sputum, the falling away of sedimentation rate and the deviation of polynuclear curve to the left. He improved, however, at the end of a short 2nd course, thus indicating the value of more than one course of treatment.

Classified result:- Improved.

## Case 4.

Leslie Marshall, age 19 years.

Commenced sanocrysin: 1st course 6.8.28. Completed 8.11.28.

" " 2nd " 16.1.29 " 27.2.29.

Duration of disease:- 6 months.

Symptoms:- Cough and spit, loss of weight, pains in chest, and slight dyspnoea on exertion.

Sputum:- T.B. ++.

Average diurnal temperature:- 97.2 - 98.6.

" " pulse rate :- 96 - 100.

Physical signs in chest:- Right side. P.N. impaired over upper lobe. Over impaired area, B.S. are broncho-vesicular and fine crepitant râles are present.  
Left side. P.N. slightly impaired over apical region; B.S. are weak and granular.

Radiogram:- (fig. 15).

Classification:- L<sub>1</sub> S<sub>2</sub> ++.

Sanocrysin given:-

1st course = .1, .2, .25, .25, .35, .35, .5, .75, .85, 1, 1, 1, 1 = 7.6 gms.

2nd " = .25, .5, .75, 1, 1, 1, 1 = 5.5 gms.

Results of treatment.

1. Average diurnal temperature:- 96.8 - 97.8.

2. " " pulse rate:- 86 - 90.

3. Weight:- Gained 1st. 8 lbs.

4. Exercise:- Full sanatorium régime.

5. Sputum:- see chart 4.

Note the gradual diminution in amount until he has no sputum on discharge. Sputum became T.B.- shortly after treatment commenced, but at end of 1st course tubercle bacilli again appeared.

6. Radiological:- (figs. 15 & 16).

Note. There is a diminution of the active 'fuzzy' nodulation in both upper lobes, the 2nd film, however, is not sufficiently 'contrasty' to be comparable.





Fig. 15. Before treatment.

Fig. 16. After treatment.

Fig. 15 demonstrates a cavity in right apex, and considerable amount of exudative disease in all lobes. Fig. 16 shows a diminution of the 'fuzzy' active disease, and increased linear fibrosis, the film, however, has been taken with a harder tube.

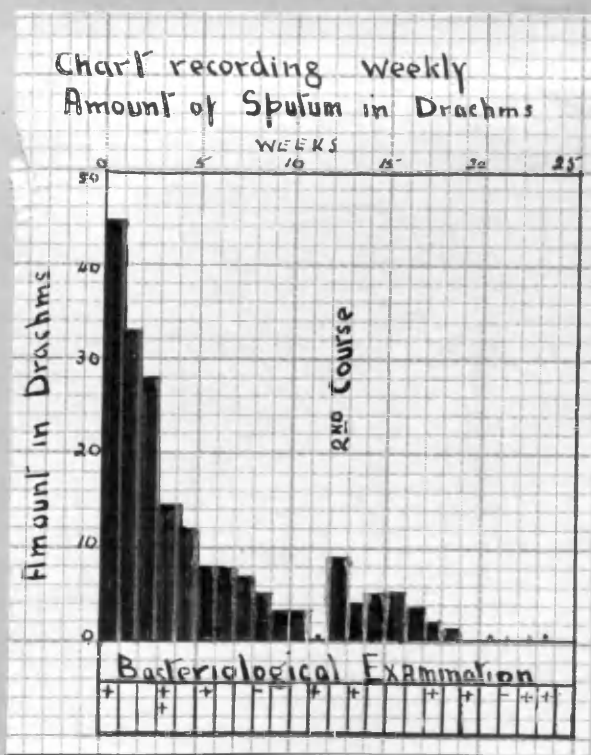


Chart 4.

# Sedimentation Rate

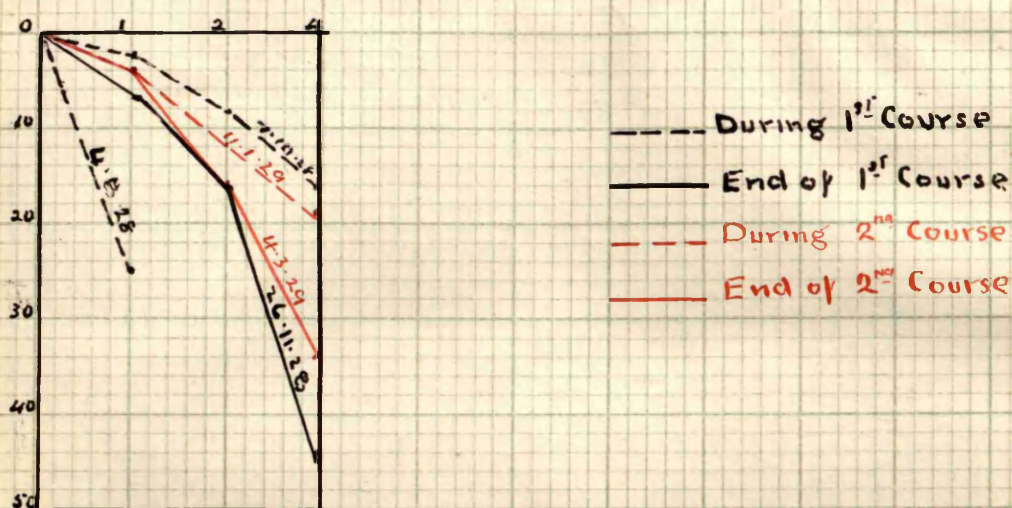


Fig. 17

# Polynuclear Count

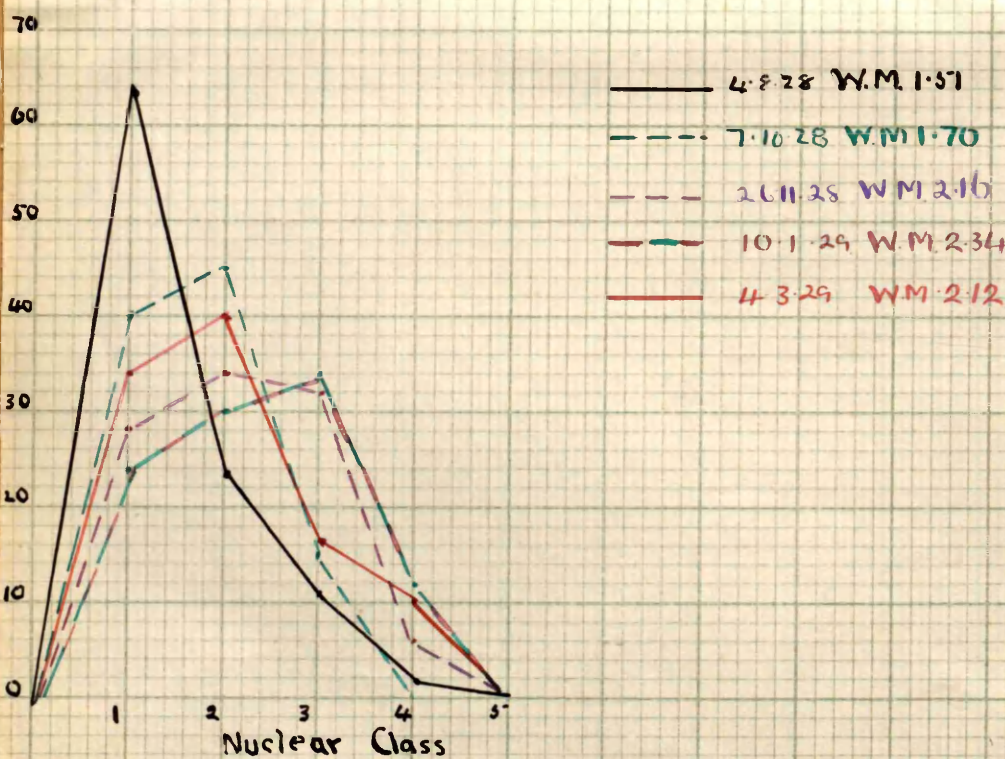


Fig. 18.

7. Physical signs:- P.N. remains impaired over both upper lobes. Expiration is slightly prolonged over both apical regions. B.S. are granular over both upper lobes.
8. Red cell sedimentation rate:- Note the improvement at end of 1st course. The improvement is maintained at end of 2nd course.
9. Polynuclear count:- Note the gradual improvement in the curves. The optimum curve is obtained at the beginning of 2nd course. At end of 2nd course the curve deviates slightly to the left.

Reactions to Sanocrysin:- (1) Focal (2) Slight albuminuria.

Resumé.

On consideration of the diminution of sputum, the gain in weight, the capacity for exercise, the improvement in the polynuclear count and the red cell sedimentation rate, there is no doubt that the patient definitely improved.

Classified result:- Improved.



## Case 5

L. H. Moore, age 22 years.

Commenced sanocrysin 1st course 29.8.28 Completed 3.12.28.

" " 2nd " 5.2.29 " 15.3.29.

Duration of disease:- 7 months.

Symptoms:- Cough, spit, night sweats and small haemoptysis.

Sputum:- T.B.+++.

Had sanatorium treatment for 8 weeks before sanocrysin commenced.

Average diurnal temperature:- 97.4 - 98.6.

" " pulse rate :- 88 + 96.

Physical signs in chest:- Right side. P.N. impaired over upper lobe. B.S. are weak. Exp.+ and fine crepitant râles are present over impaired area.

Left side. P.N. impaired over upper lobe where fine crepitant râles are present.

Radiogram:- (fig. 19).

Classification:- L<sub>2</sub> S<sub>1</sub> +++.

Sanocrysin given:-

1st course = .1, .1, .25, .35, .35, .5, .5, .75, 1, 1, 1, 1 = 6.9 gms.

2nd " = .25, .5, .75, 1, 1, 1 = 4.5 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.

2. " " pulse rate :- 80 - 82.

3. Weight:- Gained 1st. 2 lbs.

4. Exercise:- Full sanatorium régime.

5. Sputum:- see chart. 5.

Note There is diminution of sputum at end of second course.

6. Radiological:- (figs. 19 & 20).

Note the marked diminution of active 'fuzzy' nodulation in both upper lobes. After treatment both upper lobes light up much better; the peribronchial infiltration has a more defined margin, which is evidence of fibrosis.



Fig. 19. Before treatment.

Fig. 20. After treatment.

Fig. 19 shows considerable active disease in both sides.  
 Fig. 20 demonstrates the marked clearing of active nodulation.

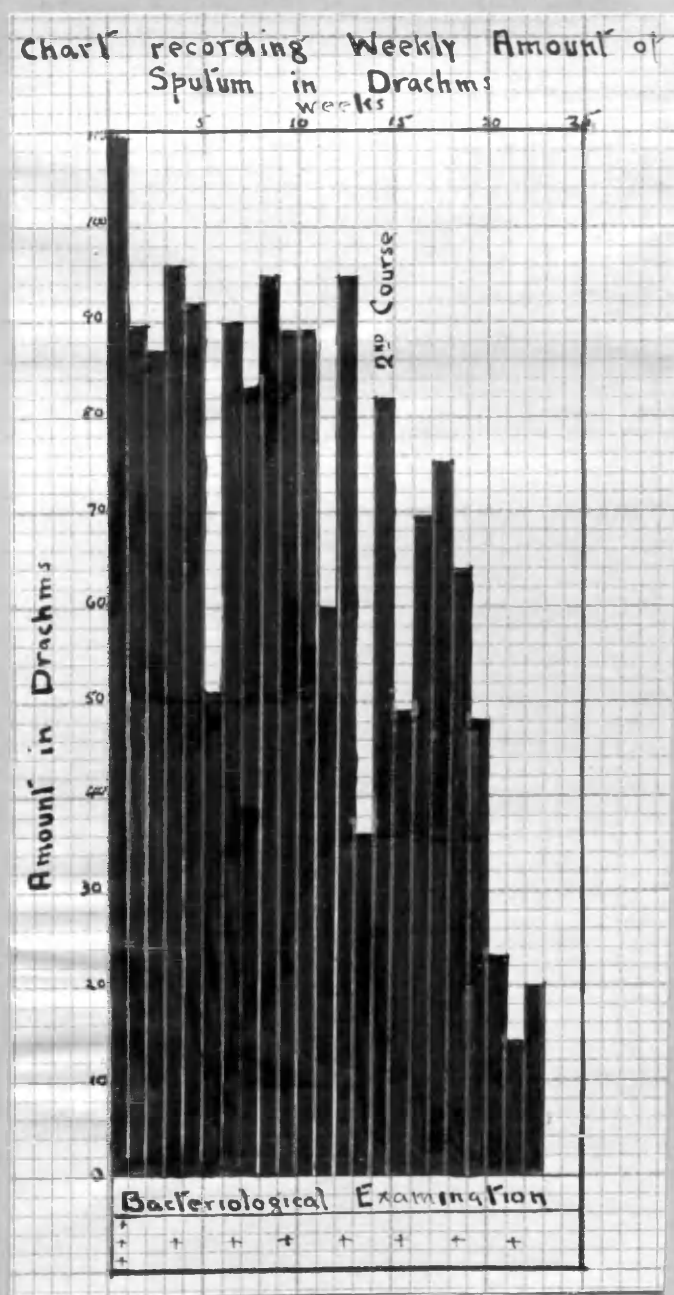


Chart 5.



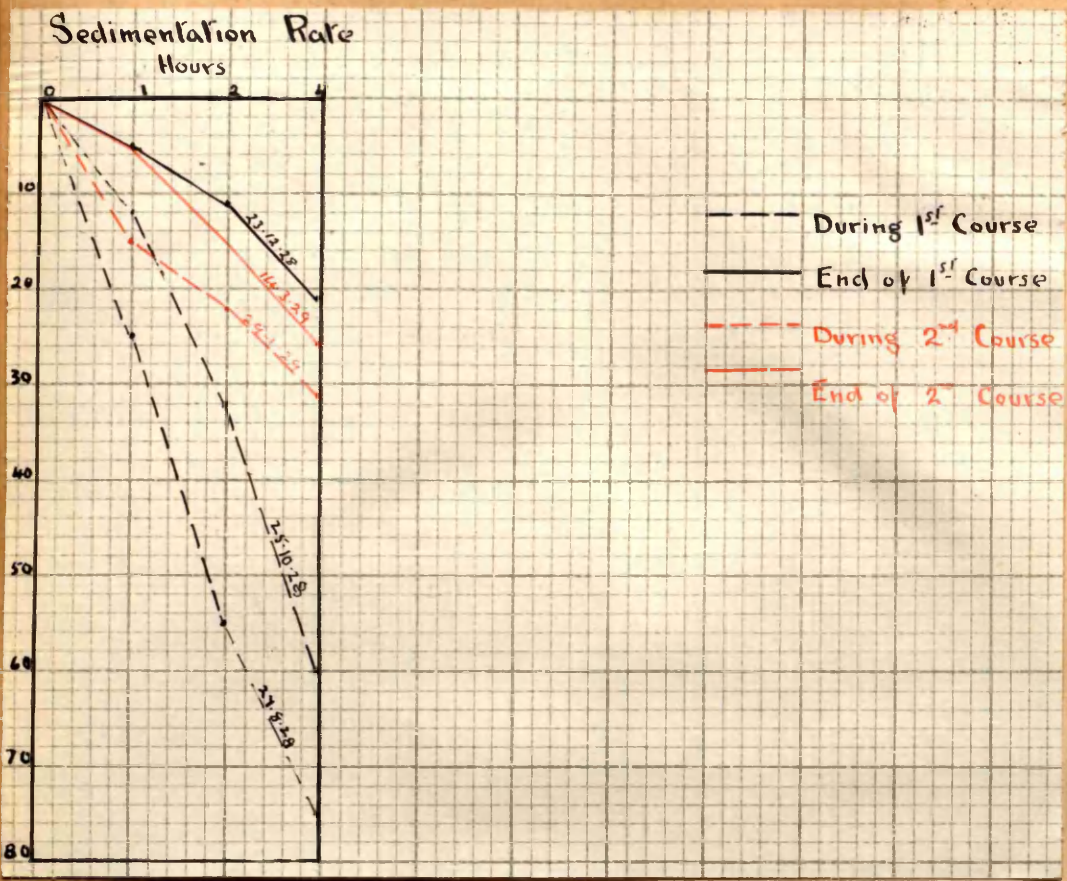


Fig. 21.

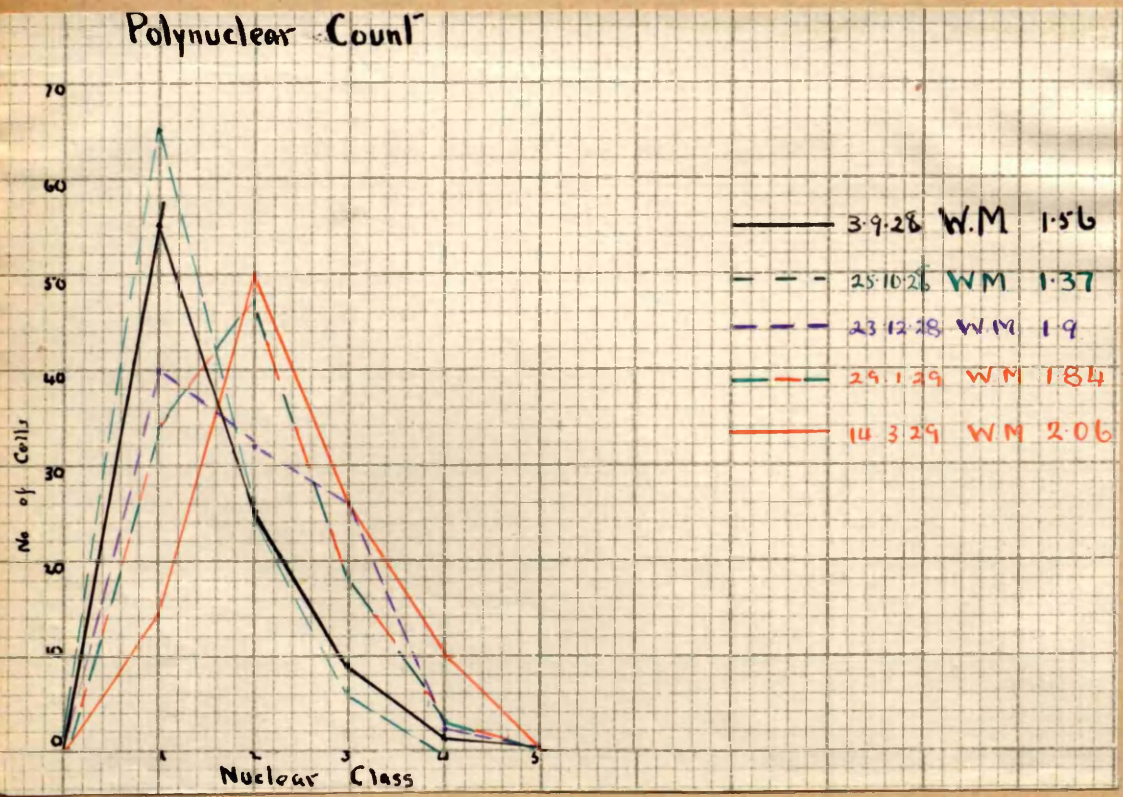


Fig. 22.

7. Physical signs:- P.N. is slightly impaired over left upper lobe. B.S. are granular over both upper lobes. Moist sounds have disappeared.

8. Red cell sedimentation rate:- (fig. 21).

Note the gradual improvement in the rate of fall.

On readmission for 2nd course, the rate increased but again improved after 2nd course.

9. Polynuclear count:- (fig. 22).

Note that the curve gradually swings over to the right, and that the weighted mean at the end of treatment is very much improved.

Reactions to sanocrysin:- (1) Focal (2) Albuminuria.

#### Resume.

This patient markedly improved, as indicated by the gain in weight, the improvement on radiological and physical examinations, and the results of the blood controls.

Classified result:- Markedly improved.

## Case 6.

John Jones      Age 20 years

Commenced Sanocrysin. 1st course 26.5.28. Completed 7.11.28.

"      "      2nd      "      22.1.29      "      27. 2.29.

Duration of disease:- 5 months.

Symptoms:- Cough and spit, loss of weight, pains in chest, and dyspnoea on exertion.

He had sanatorium treatment for 18 weeks. He continued to lose weight, and temperature remained febrile.

Sputum:- T.B.+++.

Average diurnal temperature:- 97.8 - 99.

"      "      pulse rate:- 92 - 100.

Physical signs in chest:- Right side. P.N. impaired over upper lobe. B.S. broncho-vesicular in character, and fine crepitations are present over impaired area.

Left side. P.N. impaired over upper lobe and base.

B.S. are weak. Fine post-tussive râles are audible over apical region.

Radiogram:- (fig. 23).

Classification:- L<sub>2</sub>S<sub>2</sub> +++.

Sanocrysin given:- 1st course = .05, .05, .1, .1, .1, .1, .25, .35, .35, .4, .1, .1, .25, .35, .5, .75, 1, 1 = 5.9gms.

"      "      2nd      "      = .25, .5, .75, 1, 1, 1 = 4.5 gms.

Results of treatment.

1. Average diurnal temperature:- 97 - 98.2.
2.      "      "      pulse rate :- 84 - 88.
3. Exercise:- Full sanatorium régime.
4. Weight:- Gained 1st. 2 lbs.
5. Sputum:- see chart. 6

Note the marked diminution in the quantity of sputum and in the number of bacilli present.

6. Radiological:- (figs. 23 & 24).

Note. The radiological improvement is not striking, but there is an absorption of much of the active modulation, in the right upper lobe.



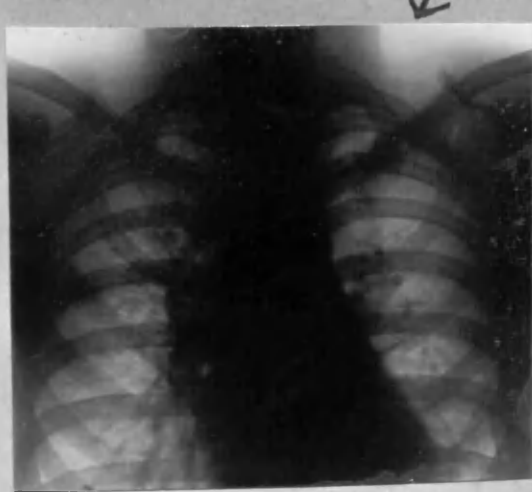
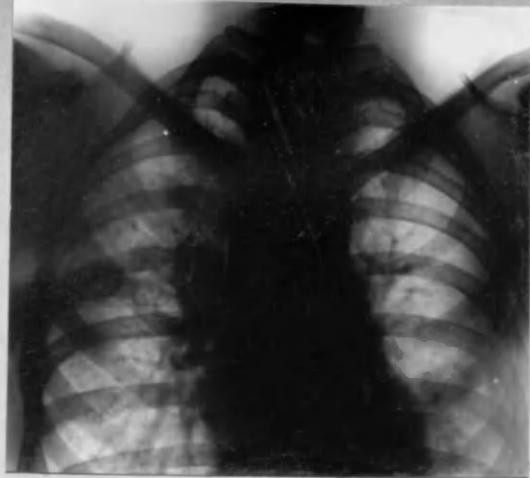


Fig. 23. Before treatment.

Fig. 24. After treatment.

Fig. 23 shows 'fuzzy' active nodulation in both upper lobes. Fig. 24 shows diminution of active disease particularly over areas indicated.

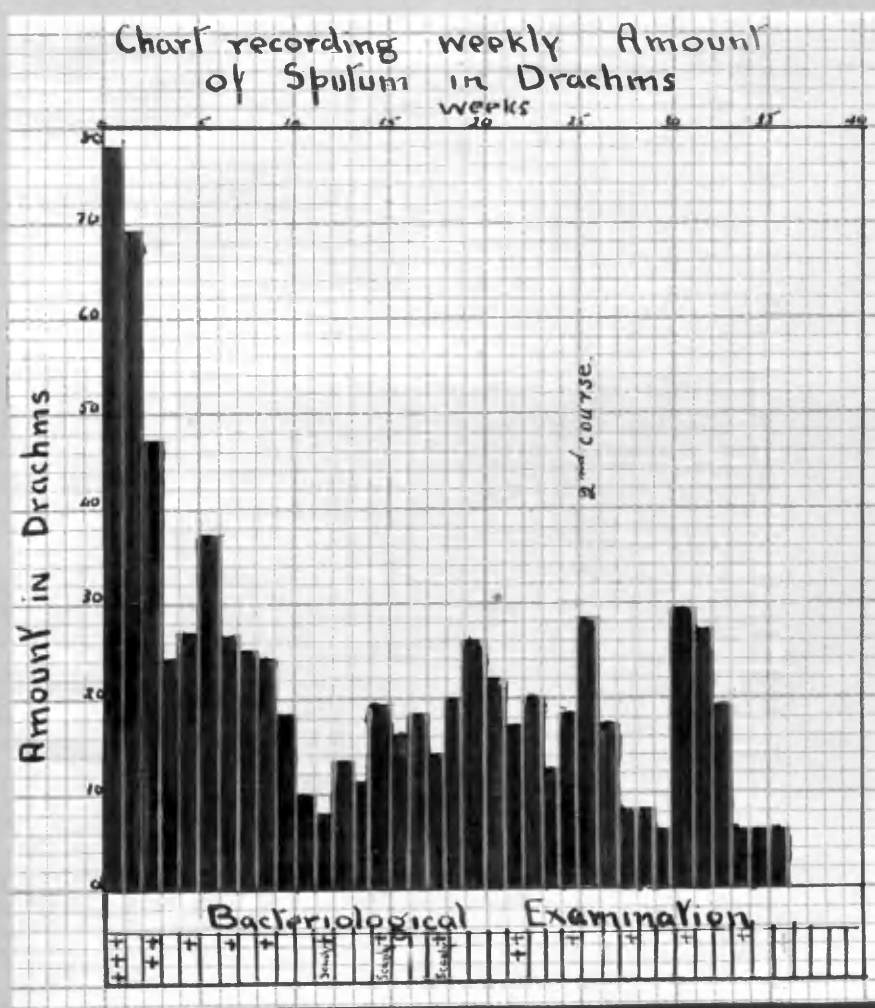
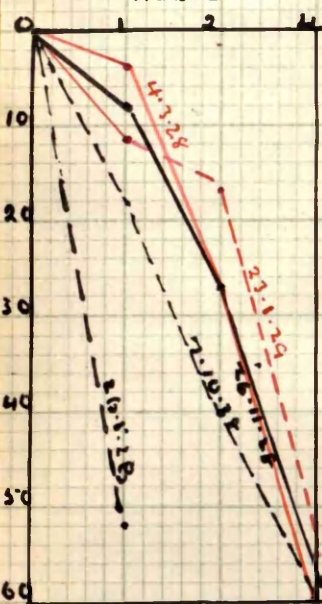


Chart 6.

# Sedimentation Rate

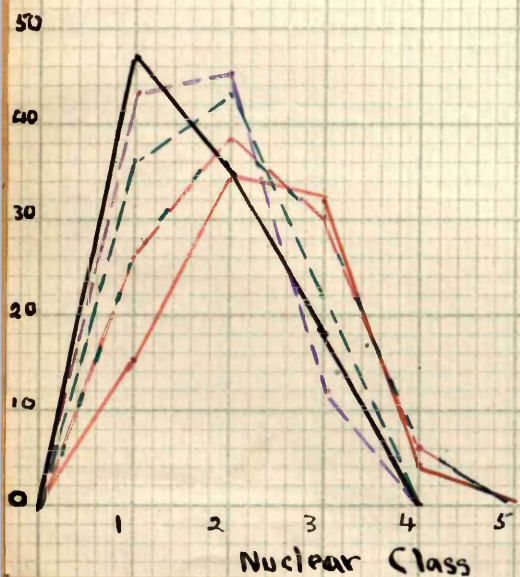
Hours



- During 1<sup>st</sup> Course
- End of 1<sup>st</sup> Course
- During 2<sup>nd</sup> Course
- End of 2<sup>nd</sup> Course

Fig. 25.

# Polynuclear Count



- 26.5.28 W.M. 1.41
- 7.10.28 W.M. 1.85
- 20.11.28 W.M. 1.69
- 14.1.29 W.M. 1.82
- 4.3.29 W.M. 1.95

Fig. 26.

7. Red cell sedimentation:- Note the gradual decrease of fall in the 1st hour, and the striking improvement at end of 2nd course.

8. Polynuclear count:- Note the gradual swinging of the curves to the right. At the end of treatment the weighted mean has considerably improved.

Reactions to Sanocrysin:- (1) Focal (2) Albuminuria

(3) Stomatitis (4) Papular rash round elbows and forearms.

#### Resume.

The treatment in this case was considerably delayed with frequent reactions. He greatly improved as is evidenced by the diminution of sputum, the capacity for exercise, the increase of weight, and the results of the polynuclear counts and sedimentation rates.

Classified result:- Improved.



## Case 7.

Mrs. Ball, age 33 years.

Commenced sanocrysin 11.12.28. Completed 21.1.29.

Duration of disease:- 1 year.

Symptoms:- Cough, spit, pains in chest, and dyspnoea on exertion.

Sputum:- T.B.+++

Average diurnal temperature:- 97 - 98.8.

" " pulse rate :- 86 - 96.

Physical signs in chest:- Left side. P.N. markedly impaired over upper lobe. Exp.+ and crepitant râles are present over impaired areas.

Right side. P.N. impaired over upper and middle lobes.

B.S. are harsh and fine râles are audible at apex.

Radiogram:- (fig. 27).

Classification:- L<sub>2</sub> S<sub>2</sub>+++

Sanocrysin given:-

.05, .1, .1, .25, .25, .35, .5, .6, .75 = 2.95 gms.

Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.
2. " " pulse rate:- 80 - 86.
3. Exercise:- Up 8 hours.
4. Weight:- I.S.Q.
5. Sputum:- see chart 7.

Note the diminution of sputum and number of bacilli present.

6. Radiological:- (figs. 27 & 28).

There is a marked increase of fibrosis and diminution of exudative disease in both upper lobes.

7. Physical signs:- P.N. remains impaired over both upper lobes, but moist sounds have considerably diminished.



Fig. 27. Before treatment.

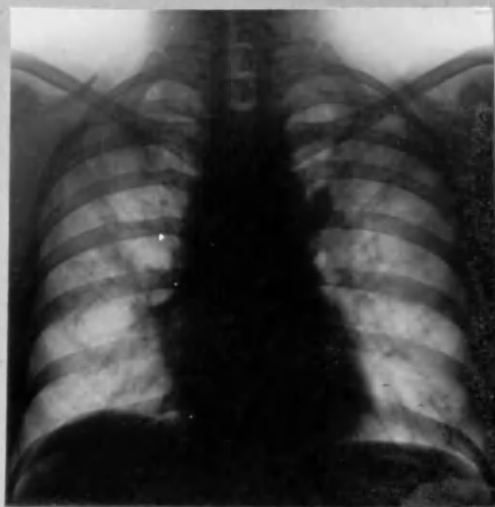


Fig. 28. After treatment.

Fig. 27 shows considerable active disease in both upper lobes particularly in the right. Fig. 28 shows a marked clearing of the active processes and general increase of fibrosis.

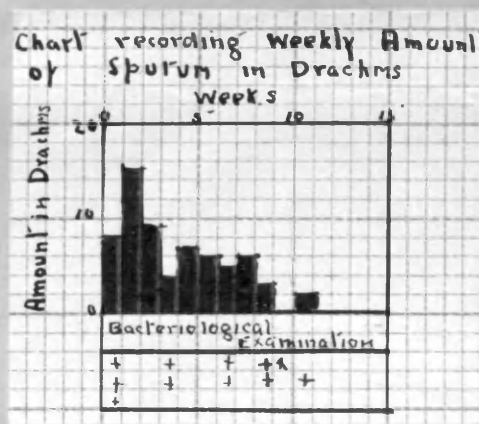


Chart 7.



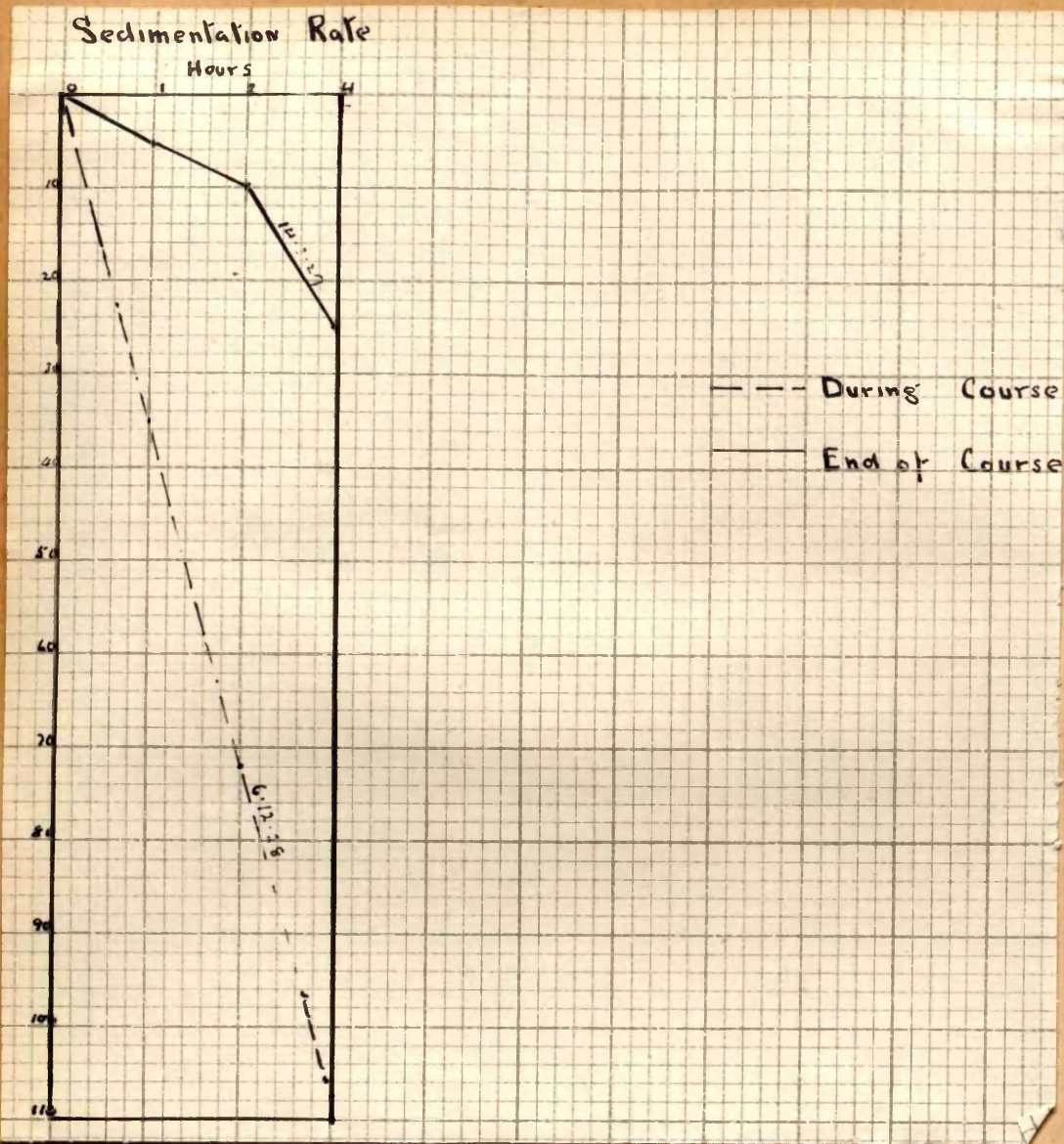


Fig. 29.

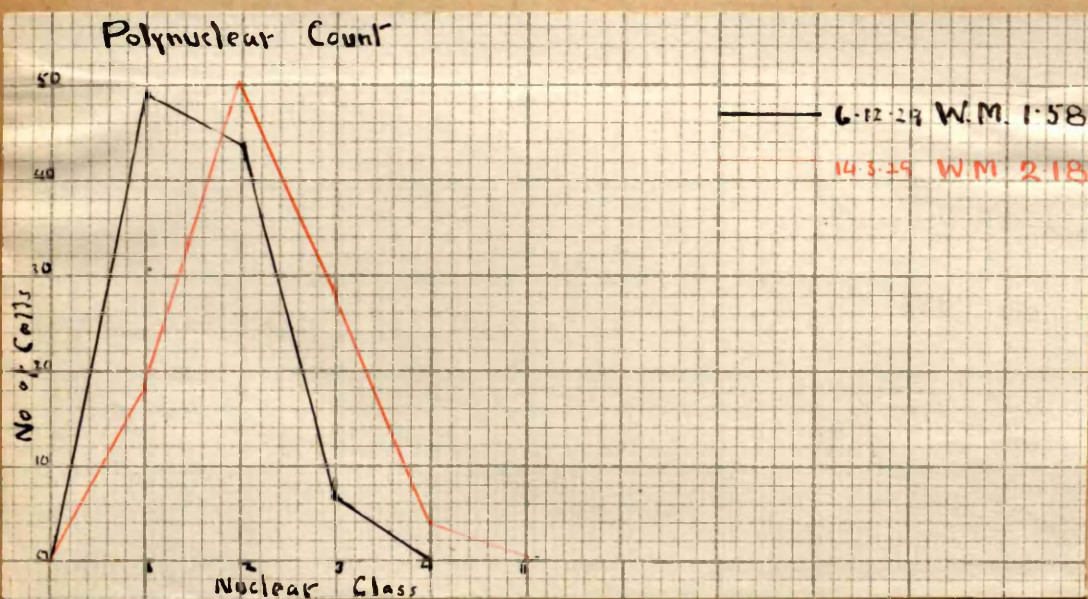


Fig. 30.

8. Red cell sedimentation rate:- (fig. 29).

Note the marked improvement in the rate at end of treatment.

9. Polynuclear count:- (fig. 30).

Note the drift of the curve to the right and the diminution of cells in Class 1 after treatment.

Reactions to sanocrysin:- (1) Focal (2) Mild dermatitis.

Resumé.

The treatment in this case was discontinued owing to the occurrence of mild dermatitis affecting the arms and chest. The chest condition, sputum, and blood controls all indicate improvement. The marked feature of the case is the improvement after a short course of sanocrysin with a fairly severe reaction.

Classified result:- Improved.

## Case 8.

Kate Bramley Age 21 years.

Commenced Sanocrysin. 1st course 25.5.28. Completed 8.9.28.

" " 2nd " 11.12.28. " 31.1.29.

Duration of disease:- 1 year.

Symptoms:- Cough and spit, pains in chest, night sweats, loss of weight, and dyspnoea on exertion.

Sputum:- T.B.+++.

Average diurnal temperature:- 97.6 - 99.6.

" " pulse rate :- 80 - 96.

Physical signs in chest:- Right side. P.N. impaired over upper and middle lobes. Expiration is prolonged over impaired area.

Crepitant râles are present.

Left side. P.N. impaired over upper lobe. B.S. weak.

Fine moist râles audible.

Radiogram:- (fig. 31 ).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:-

1st course = .05, .05, .1, .1, .2, .3, .5, .6, .75, .75, .85, .85, .95,  
                  .85, .85 = 7.75 gms.

2nd " = .1, .25, .5, .75, .75, 1, 1, 1 = 5.35 gms.

Results of treatment.

1. Average diurnal temperature:- 97 - 98.2.
2. " " pulse rate :- 76 - 80.
3. Exercise:- Full sanatorium régime.
4. Weight:- Gained 5 lbs.
5. Sputum:- see chart. 8.

Note. Marked diminution and ultimately no sputum.

6. Radiological:- (figs. 31 & 32).

Note in the right upper and middle lobes, the diminution of fuzziness, the increase of fibrosis, and evidence of compensatory emphysema. In left upper lobe the radiological improvement is very slight.



Fig. 31. Before treatment.



Fig. 32. After treatment.

Fig. 31 shows a marked amount of fibro-exudative disease in right upper lobe and also infiltrative disease in left side. Fig. 32 demonstrates a diminution of active disease and increase of fibrosis; this is seen better in the original films.

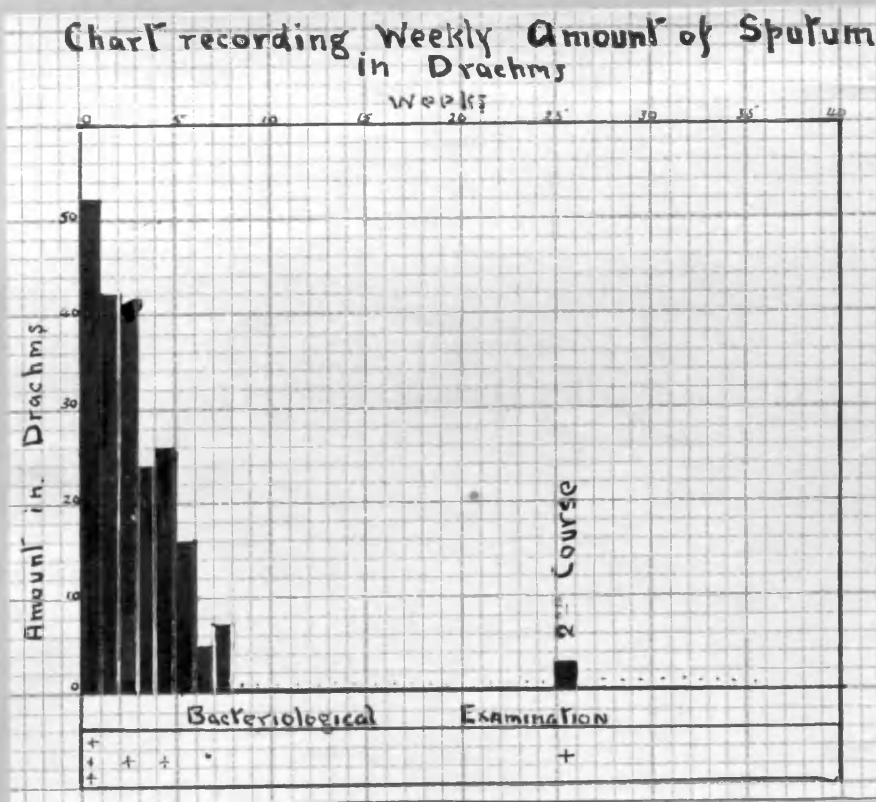


Chart 8.



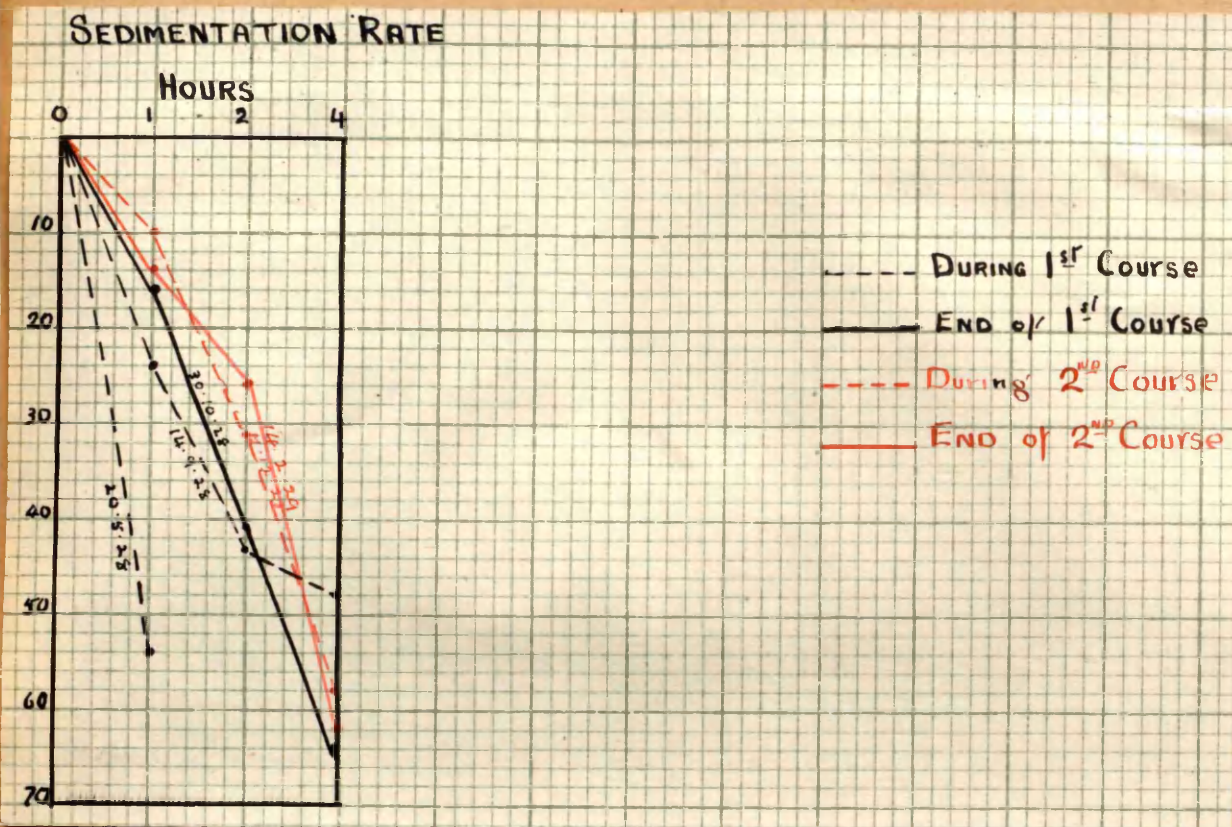


Fig. 33.

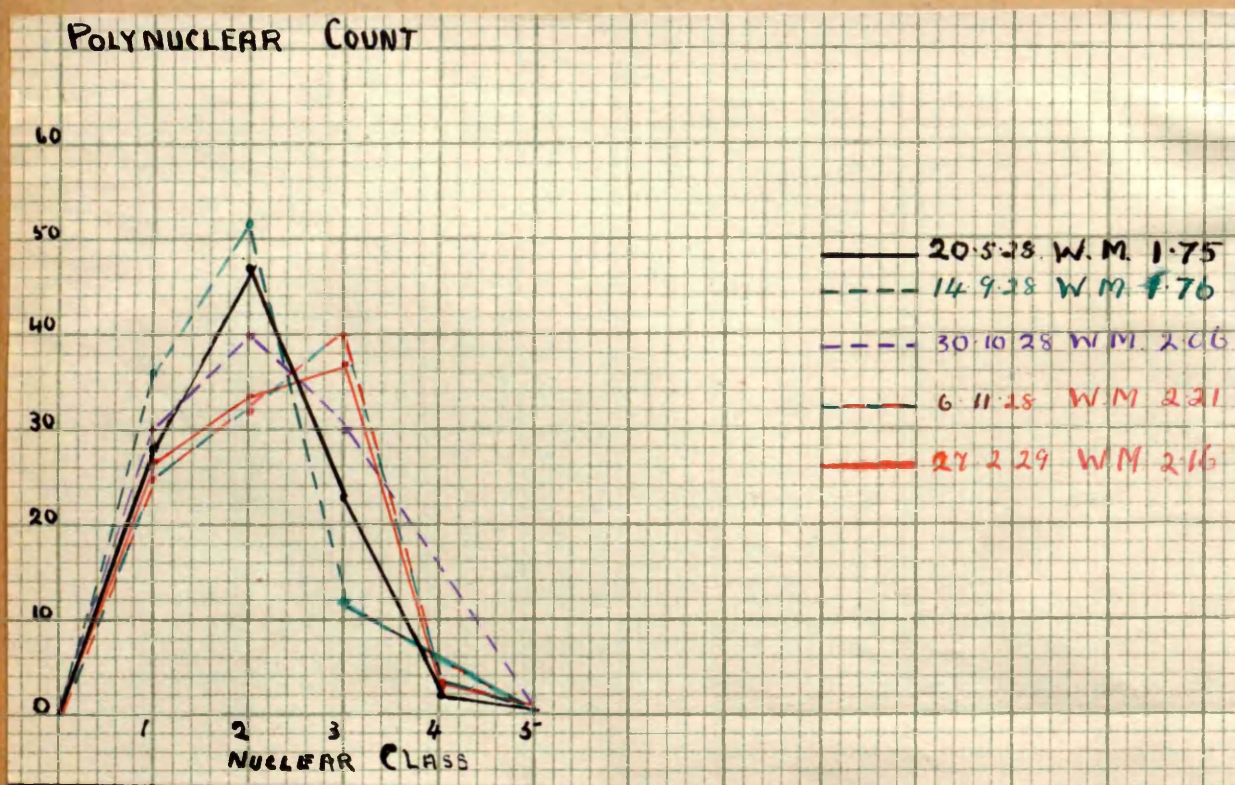


Fig. 34.

7. Physical signs:- Moist sounds gone. Evidence of compensatory emphysema on right side. B.S. weak over right upper lobe.
8. Red cell sedimentation rate:- The rate gradually improves until the end of 1st course. At the commencement of 2nd course the improvement is maintained, and at the end of this course, the curve falls away. This is probably due to the fact that the patient had gastrointestinal disturbance.
9. Polynuclear count:- Note the gradual swerving of the curves to the right. At the end of treatment the weighted mean is slightly less than that at the commencement of 2nd course.

Reactions to Sanocrysin:- (1) albuminuria (2) Vomiting and diarrhoea after final injections of 1 gramme.

#### Resumé.

This patient improved as shown by the physical signs, afebrile temperature, diminution of sputum, polynuclear counts and sedimentation rates. The slight falling away of the sedimentation rate and polynuclear count, at the completion of 2nd course, is probably due to gastrointestinal disturbance.

Classified result:- Markedly improved.

## Case 9.

Hilda Lees aged 18 years.

Commenced Sanocrysin. 1st course 17.7.28. Completed 13.11.28.

" " 2nd " 16.1.29 " 5.3.29.

Duration of disease:- 6 months.

Symptoms:- Cough, blood stained spit, loss of weight, dyspnoea and haemoptysis.

Sputum:- T.B.+.

Average diurnal temperature:- 98 - 99.4.

" " pulse rate :-110 - 120.

Physical signs in chest:- Right side. PnN. impaired over upper and middle lobes where Exp.+ and fine post-tussive rales are present.

Left side. P.N. impaired over lower lobe. B.S. are faint, and numerous crepitations are present over impaired area.

Radiogram:- (fig. 35).

Classification:- L<sub>2</sub> S<sub>2</sub> +

Sanocrysin given:-

1st course = .05, .05, .1, .1, .1, .2, .25, .25, .35, .35, .35, .5, .5, .75, .75, .85, 1, 1 = 7.7 gms.

2nd " = .25, .5, .75, .75, .75, .85, .85 = 4.7 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.2.

2. " " pulse rate :- 92 - 96.

3. Exercise:- Full sanatorium regime.

4. Weight:- Gained 2 stones.

5. Sputum:- See chart.9.

Note the diminution of sputum at end of 1st course and recurrence on commencement of 2nd course.

6. Radiological:- (figs. 35 & 36).

There is an increase of fibrosis and marked diminution in the active disease in the right upper and left lower lobes.



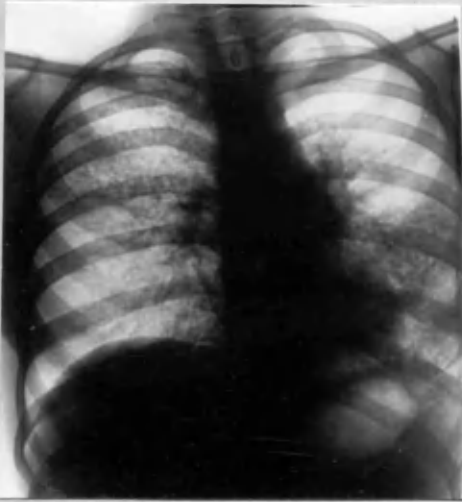


Fig. 35. Before treatment.

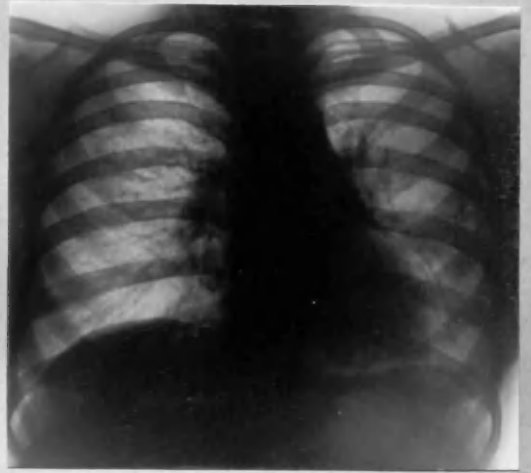


Fig. 36. After treatment.

Note in Fig. 35, the heart pulled over to the left, and the extensive active nodulation in left lower and right upper lobes. Fig. 36 demonstrates marked clearing of the extensive exudative disease.

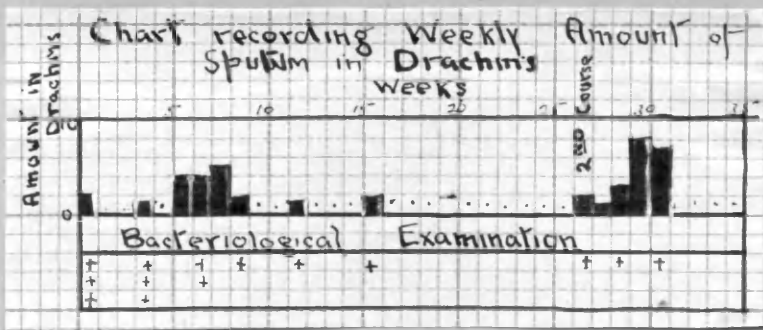


Chart 9.



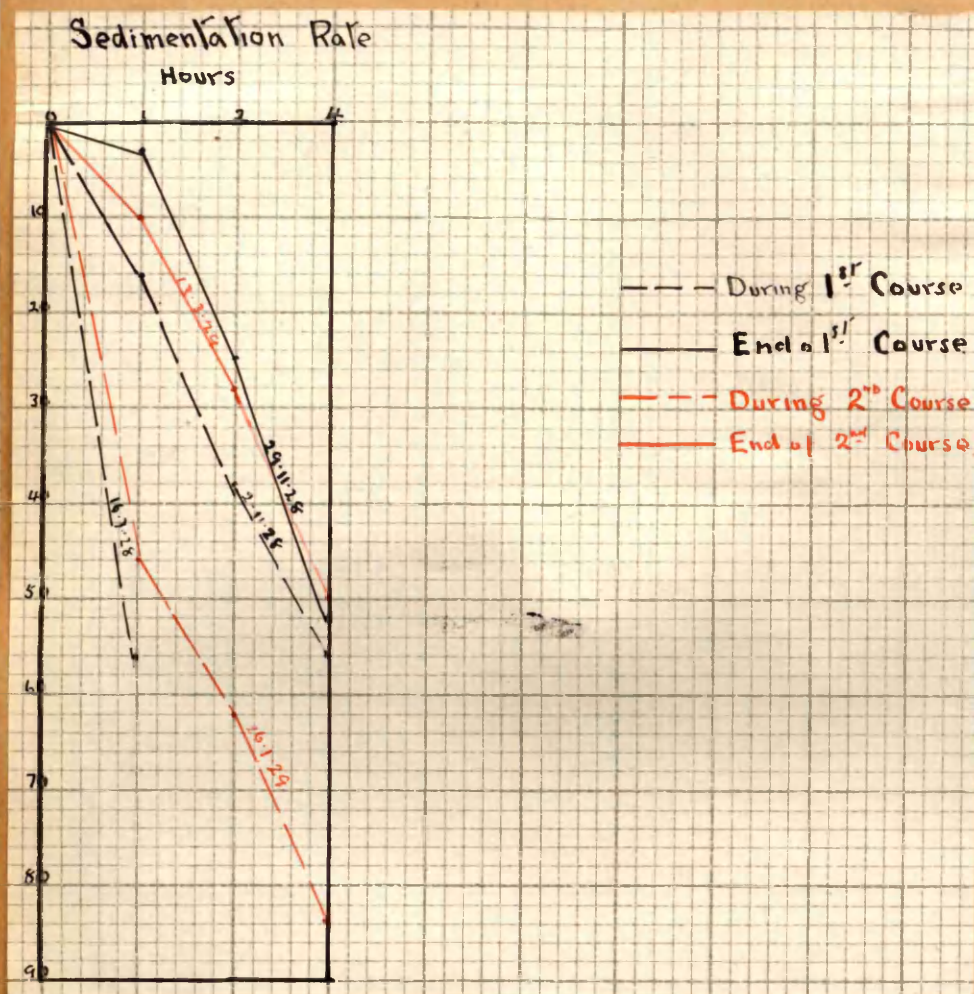


Fig. 37.

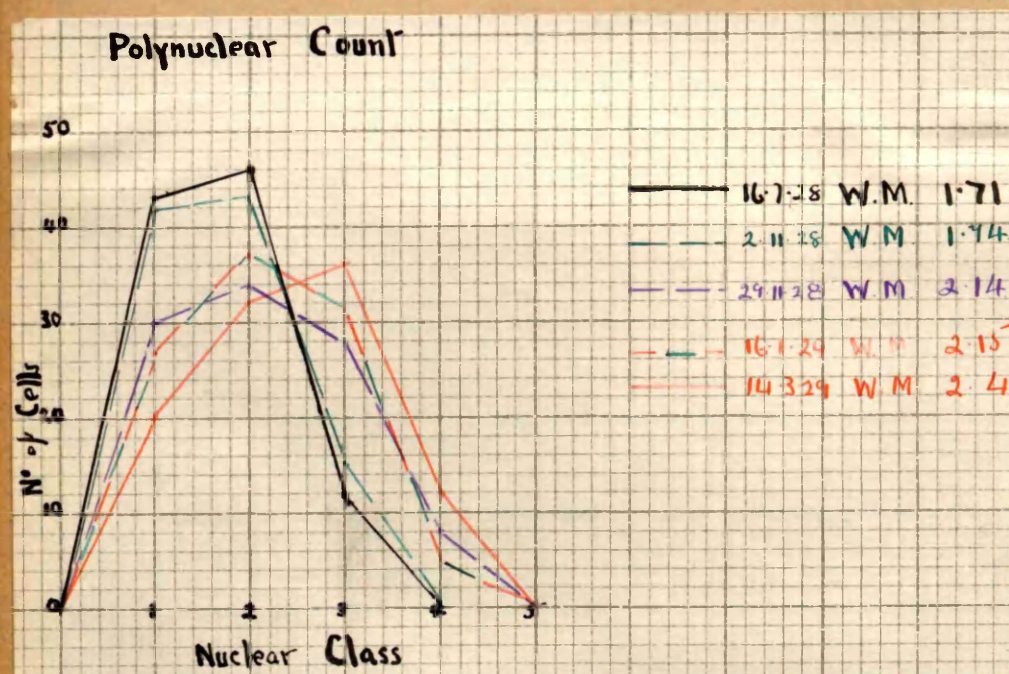


Fig. 38.

7. Physical signs:- The percussion note is not so markedly impaired over right upper and left lower lobes. B.S. are harsh at both bases, and fine post-tussive râles are still audible over left lower lobe.

8. Red cell sedimentation rate:- (fig. 37).

Note the improvement at the end of 1st course. At commencement of 2nd course the rate in the 1st hour increased, but improved at the end of 2nd course.

9. Polynuclear count:- (fig. 38).

Note the gradual improvement in the curve until a normal curve is obtained at the end of treatment.

Reactions to sanocrysin:- (1) Focal.

#### Resume.

This patient improved markedly in general condition. The improvement is indicated by the gain in weight, the exercise tolerance, the results of radiological and physical examinations, and the blood controls.

The polynuclear counts demonstrate a gradual improvement. The unfavourable feature of the sedimentation rate is the steep fall on readmission for 2nd course, the rate, however, improved at the end of 2nd course, indicating the value of several courses of treatment.

Classified result:- Markedly improved.

## Case 10

Mrs. Colby age 25 years.

Commenced Sanocrysin. 1st course 17.7.28 Completed 17.11.28.

" " 2nd " 16.1.29 " 12.3.29.

Duration of disease:- 8 months.

Symptoms:- Cough, spit, and rapid loss of weight.

Remained on rest for 20 weeks and was obviously going downhill before sanocrysin commenced.

Sputum:- T.B.+++.

Average diurnal temperature:- 97.2 - 99.2.

" " pulse rate :- 84 - 96.

Physical signs in chest:- Right side. P.N. dull over upper and middle lobes. Tubular breathing with faint w.p. in subclavicular region. Numerous medium moist râles over scapular area.

Left side. P.N. slightly impaired at apex. B.S. granular.

Radiogram:- (fig. 39 ).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:- 1st course = .05, .05, .05, .1, .1, .15, .25, .25,

.35, .35, .35, .5, .5, .75, .75, .75, .75, .85, .85 = 7.75

" " 2nd course = .25, .5, .75, .75, .85, .85, .85, .85 = 5.65

#### Results of treatment.

1. Average diurnal temperature:- 97 - 98.

2. " " pulse rate :- 80 - 86.

3. Weight:- Gained 1½ stones.

4. Exercise:- Full sanatorium régime.

5. Sputum:- see chart. 10.

Note the marked diminution of sputum after treatment.

Sputum remained T.B. + throughout, although the number of bacilli were markedly reduced.

6. Radiological:- (figs. 39 & 40).

Note the marked increase of fibrosis and the reduction in the size of the cavity, in the right upper lobe.



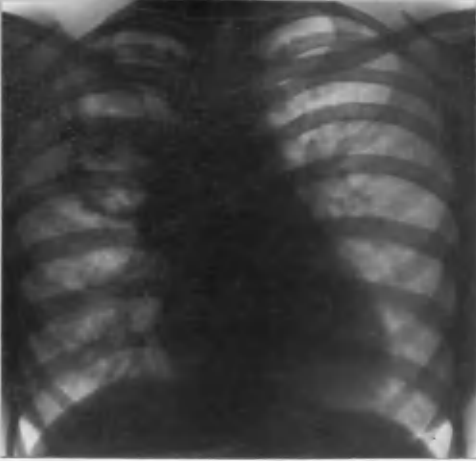


Fig. 39. Before treatment.



Fig. 40. After treatment.

Fig. 39 shows fibro-exudative disease in both sides, and a large cavity in right upper lobe.  
 Fig. 40 demonstrates clearing of active nodulation, increase of fibrosis, and shrinkage of the cavity.

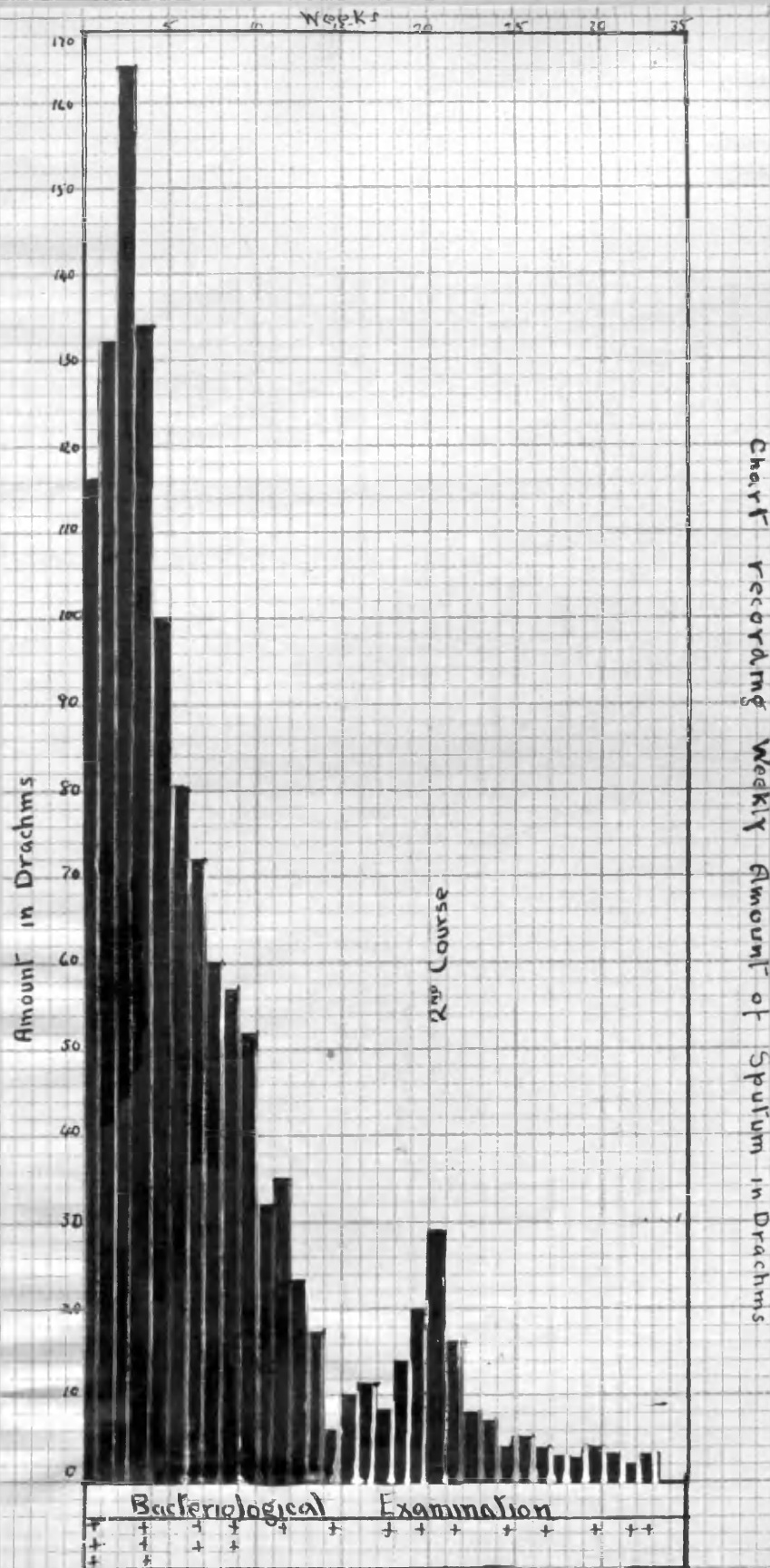


Chart 10.



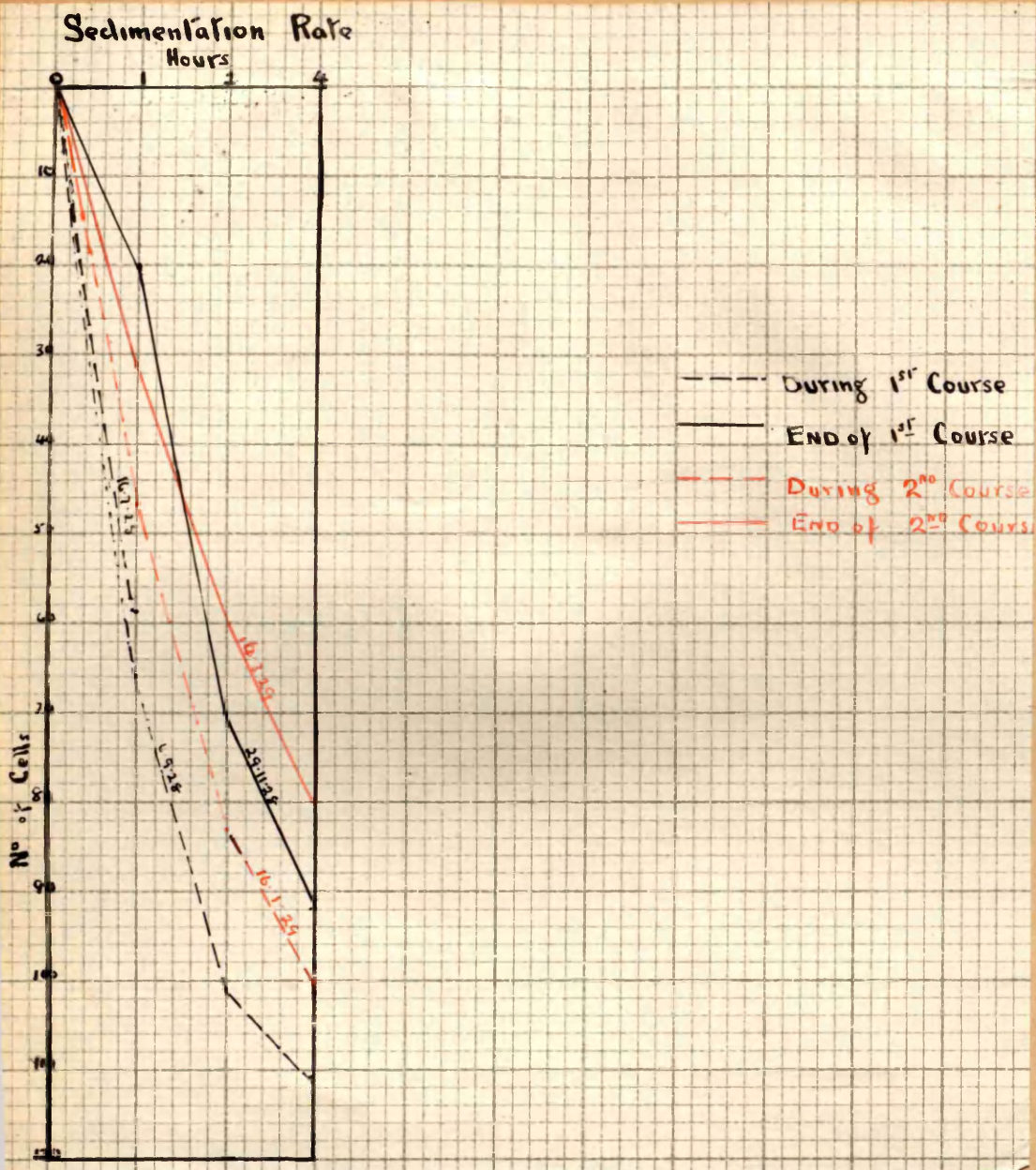


Fig. 41

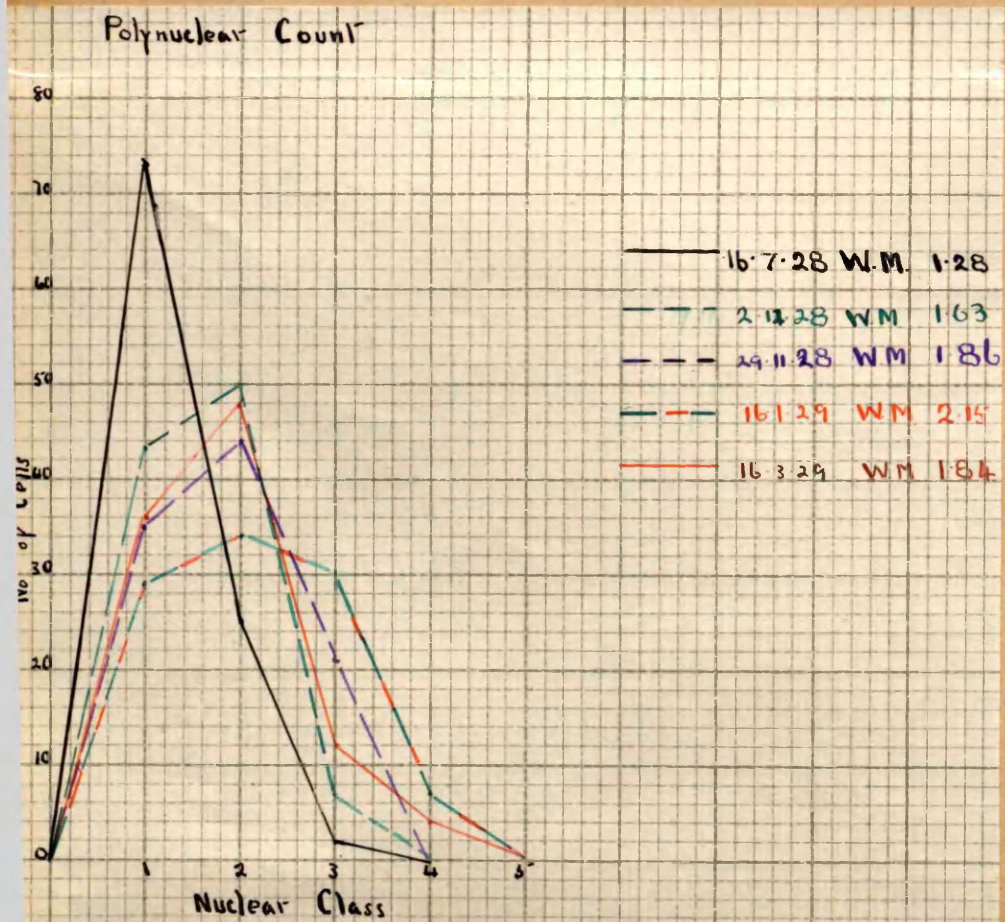


Fig. 42.

7. Physical signs:- Signs of compensatory emphysema on left side, moist sounds have gone from right side; bronchial breathing is present at apex.

8. Red cell sedimentation rate:- (fig. 41).

Note the steep fall on commencement of treatment, and the improvement at end of 1st course. At end of 2nd course the initial improvement is not fully maintained.

9. Polynuclear count:- (fig. 42).

Note the gradual diminution of cells in Class I. The optimum curve is obtained at the commencement of 2nd course.

Reactions to sanocrysin:- (1) Focal.

### Resumé.

The improvement in the general condition of this patient is very striking; this is evidenced by the increase of weight, the diminution of sputum and the exercise tolerance.

The results of the sedimentation rates and polynuclear counts, however, indicate that immediate improvement has taken place, but the ultimate prognosis should be guarded.

Classified result:- Improved.

Case 11.

Mrs. McCabe, age 31 years.

Commenced Sanocrysin 17.7.28. Completed 17.1.29.

Duration of disease:- 2 years.

Symptoms:- Cough and spit, becoming progressively worse, loss of weight, and dyspnoea on exertion.

Average pulse rate:- 96

Average diurnal temperature:- 98 - 100

Sputum:- T.B.+++.

Physical signs in chest :- Right side. P.N. markedly impaired over upper and middle lobes where vesico-bronchial breathing, V.R.++, and fine crepitant râles are present. Left side. P.N. impaired over upper lobe and fine post tussive crepitations are present.

Air entry is diminished at bases.

Radiogram:- (fig. 43)-

Classification:- L<sub>2</sub> S<sub>2</sub> +++

Sanocrysin given = .95, .05, .05, .1, .1, .2, .2, .1, .2, .35, .5, .5, .75, .75, .75, .75, .75, .75 = 6.9 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97 - 98.
2. " " pulse rate :- 76 - 84.
3. Exercise:- Walks and light ward work.
4. Weight:- Gained 7½ lbs.
5. Sputum:- see chart. 11.
6. Note. Marked diminution in weekly amount of sputum.  
Sputum never free from tubercle bacilli although numbers are considerably reduced.
6. Radiological:- (figs. 43 & 44).  
Note. Diminution in amount of exudative disease, and increase of fibrosis in right upper and middle lobes. After treatment the cavity at right apex is smaller and has a more defined outline.



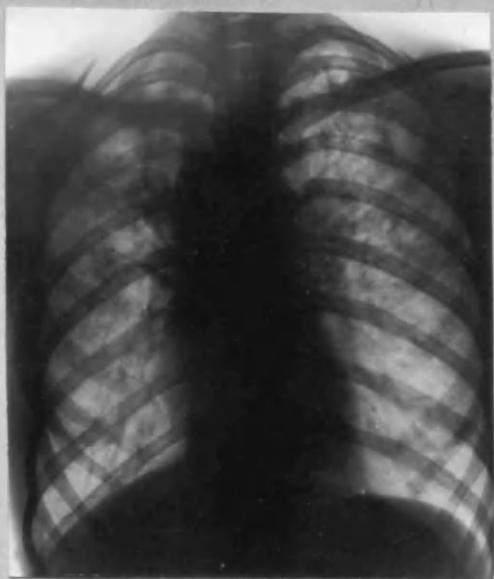


Fig. 43. Before treatment.

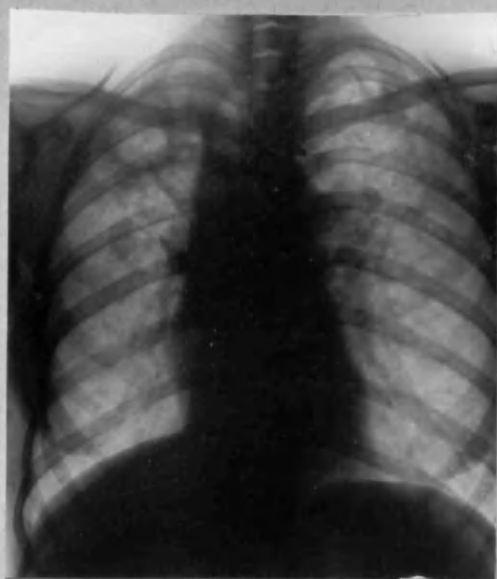


Fig. 44. After treatment.

Fig. 43 demonstrates a blurred outline of a cavity in right upper lobe. There is a considerable amount of fibro-exudative disease in both sides particularly in the right. Fig. 44 shows a shrinkage in the size of the cavity and considerable clearing of the active processes.

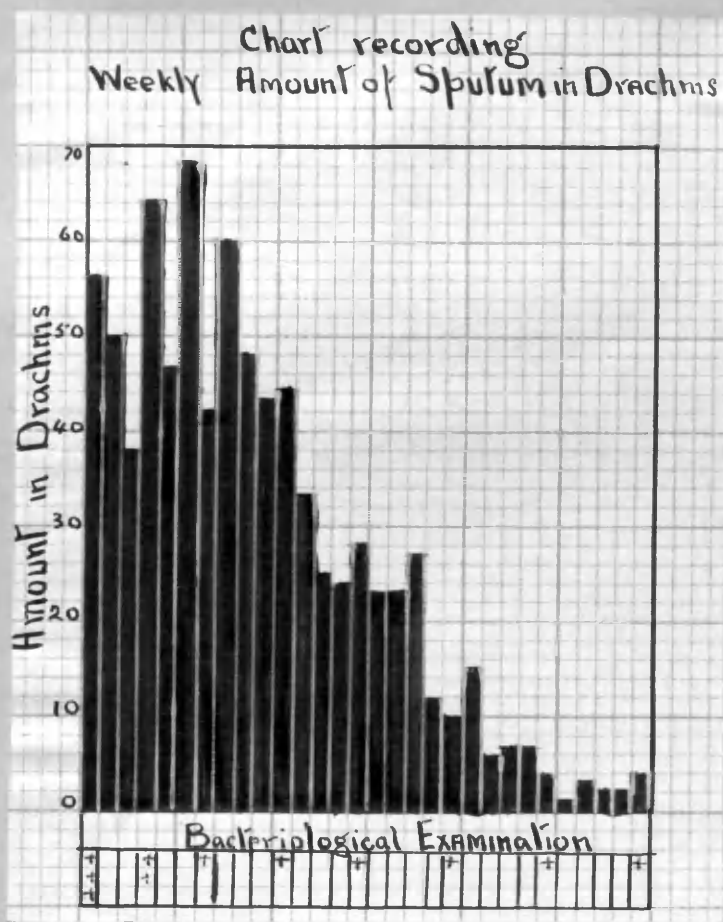


Chart 11.



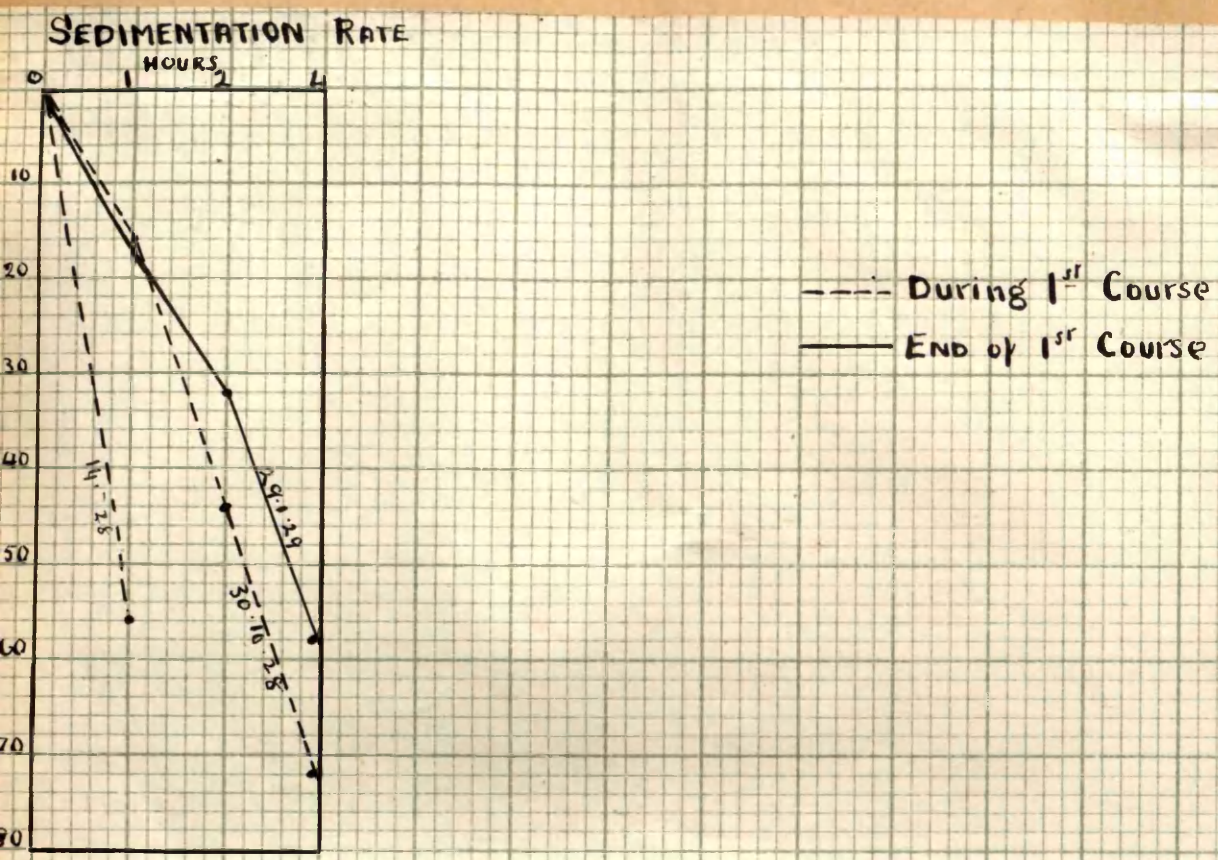


Fig. 45.

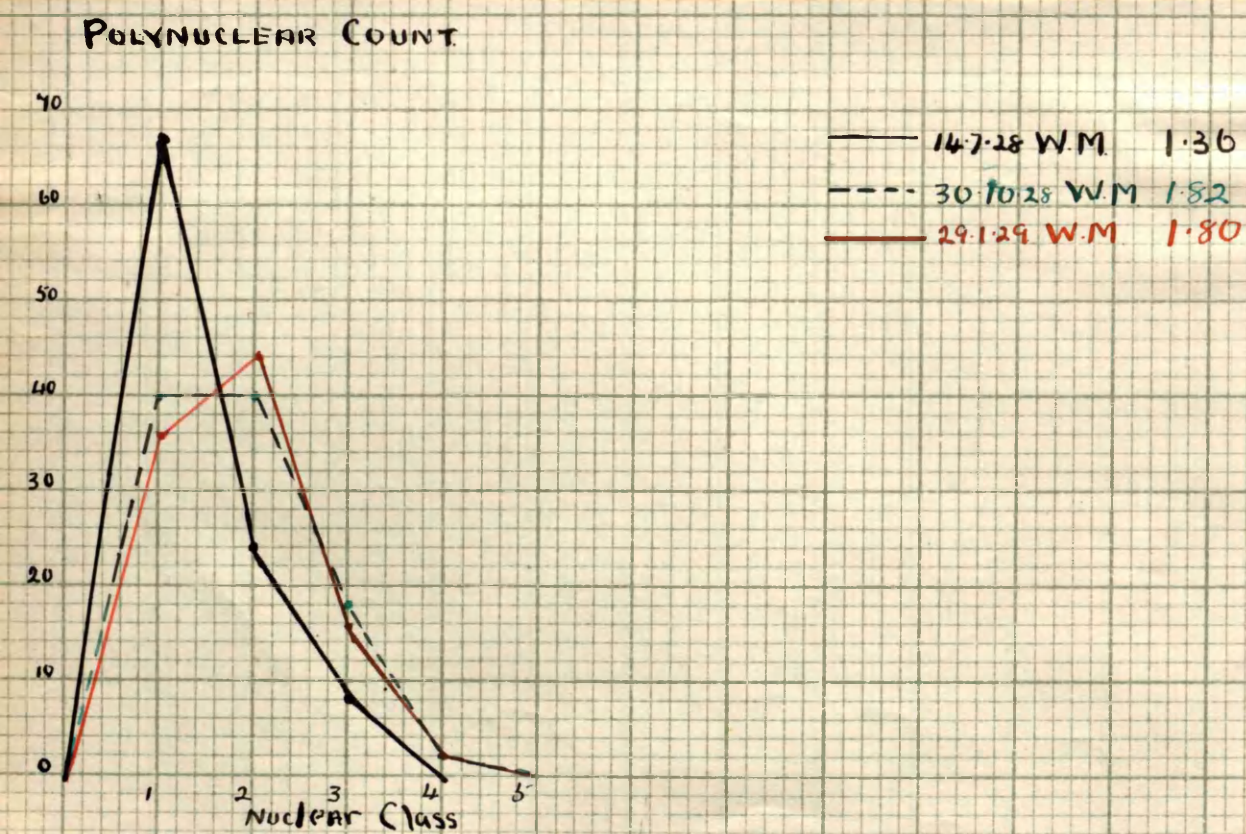


Fig. 46.

7. Physical signs:- P.N. remains impaired over right upper lobe, but no adventitious sounds present. B.S. weak over left upper lobe. Air entry has improved at bases.
8. Red cell sedimentation rate:- Note the steep drop in the 1st hour at the commencement of treatment, and the improvement on completion of 1st course.
9. Polynuclear count:- Note the swinging of the curve to the right, and the drop in the number of **cells** in the 1st group after treatment. Curve still remains abnormal.
- Reactions to sanocrysin:- (1) Focal (2) Stomatitis (3) Transient papulo erythematous rash round elbows.

Resumé.

Treatment in this case was delayed owing to frequent stomatitis after larger doses. As the result of treatment she became afebrile, and able to perform exercise grade. She undoubtedly improved, but the sedimentation rate and polynuclear count indicate that there is room for further improvement.

Classified result:- Improved.

## Case 12

Dorothy Newby age 20 years.

Commenced sanocrysin 1st course 27.5.28. Completed 12.11.28..

" " 2nd " 4.2.29. " 16.3.29.

Duration of disease:- 7 months.

Symptoms:- Cough and spit, occasional night sweats, loss of weight and dyspnoea on exertion.

Sputum:- T.B.+++.

Had sanatorium treatment for 32 weeks and condition remained unsatisfactory.

Average diurnal temperature:- 97 - 99.

" " pulse rate :- 90 - 112.

Physical signs in chest:- Right side. P.N. markedly impaired over upper lobe. Vesico-bronchial breathing over impaired area, where pleural creaks and fine crepitations are audible. Left side. P.N. impaired over upper lobe, where fine crepitant râles are audible.

Radiogram:- (fig. 47).

Classification:- L<sub>2</sub> S<sub>2</sub> +++.

Sanocrysin given:-

1st course = .05, .05, .1, .1, .2, .2, .3, .4, .5, .75, .6, .5, .75, .75, .75 = 6.0

2nd " = .1, .25, .5, .75, .85, .85, .85 = 4.15 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.2.

2. " " pulse rate:- 82 - 88.

3. Weight:- Gained 14 lbs.

4. Exercise:- Full sanatorium régime.

5. Sputum:- see chart.12.

Note the complete absence of sputum on completion of treatment. The sputum became negative for tubercle bacilli shortly after commencement of treatment, but again became positive on readmission for 2nd course.

6. Radiological:- (figs.47 & 48).

Note the marked diminution of exudative disease and increase of fibrosis on both sides.





Fig. 47. Before treatment.

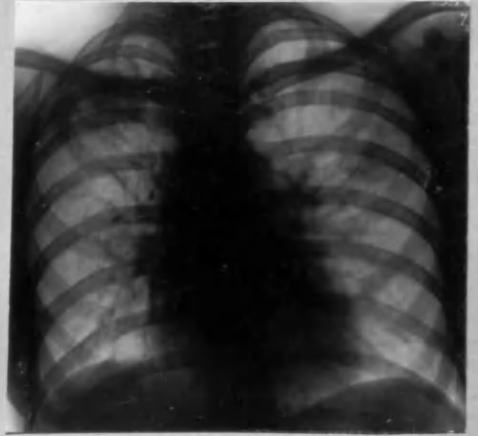


Fig. 48. After treatment.

Fig. 47 shows considerable 'fuzzy' active nodulation in all lobes, the right upper lobe being severely affected. Fig. 48 demonstrates remarkable radiological clearing of active disease.

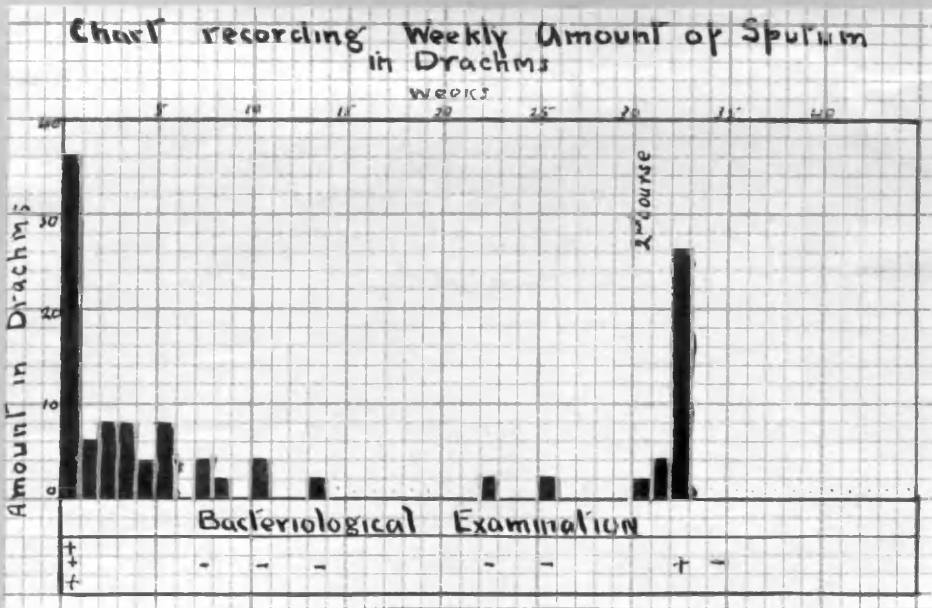


Chart 12.

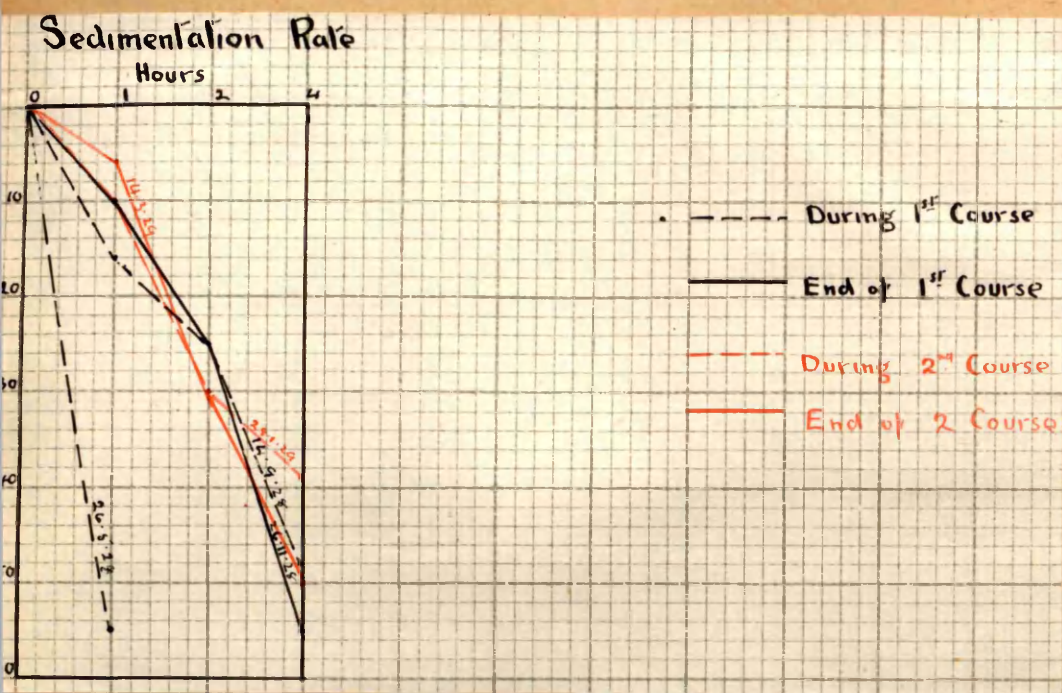


Fig. 49.

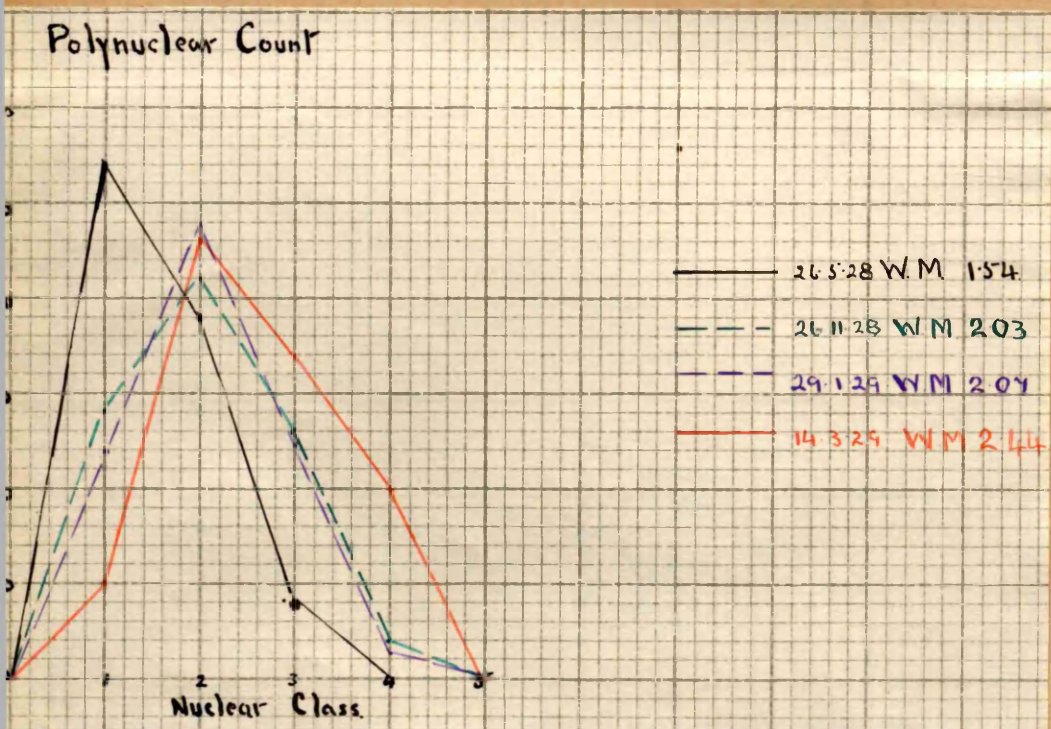


Fig. 50.

7. Physical signs:- Right side. P.N. impaired at apex where broncho-vesicular breathing is present .  
No adventitious sounds audible.  
Left side. P.N. slightly impaired at apex. B.S. are weak, and a distant rhonchus is heard. Moist sounds have disappeared.
8. Red cell sedimentation rates:- (fig. 49).  
Note the gradual improvement in the rate of fall in the 1st hour. The optimum rate occurs on completion of 2nd course.
9. Polynuclear count:- (fig. 50).  
Note the gradual improvement in the curve until the normal curve is obtained on completion of treatment.
- Reactions to sanocrysin:- (1) Focal (2) Stomatitis  
(3) Slight albuminuria (4) Multiple boils.

#### Resume.

Treatment in this case was delayed owing to the frequent occurrence of stomatitis. She improved markedly at the end of 1st course, and no reactions occurred during the 2nd course.

The marked improvement is indicated by the blood controls, the radiological and physical examinations, the exercise tolerance, the gain in weight and the diminution of sputum.

Classified result:- Markedly improved.



## Case 13.

Arthur Wykes, age 18 years.

Sanocrysin commenced 12.12.28. Completed 11.3.29.

Duration of disease:- 6 months.

Symptoms:- Cough and spit, night sweats, loss of weight, dyspnoea on exertion, and one haemoptysis.

Sputum:- T.B.+++.

Had sanatorium treatment for 12 weeks before sanocrysin commenced.

Average diurnal temperature:- 97 - 98.8.

" " pulse rate:- 96 - 100.

Physical signs in chest:- Right side. P.N. impaired over upper lobe. B.S. are very weak; fine crepitant râles are audible over impaired area.

Left side. P.N. impaired over upper lobe. Fine crepitant râles present over impaired area.

Radiogram:- (fig. 51).

Classification:- L<sub>2</sub> S<sub>2</sub> ++.

Sanocrysin given:-

·05, ·1, ·25, ·35, ·35, ·35, ·5, ·75, ·75, ·85, ·85, 1, 1 = 7.15 gms.

Results of treatment.

1. Average diurnal temperature:- 97 - 98.2.

2. " " pulse rate :- 82 - 86.

3. Weight:- Gained 10 lbs.

4. Exercise:- On full/sanatorium régime.

5. Sputum:- see chart 13.

Sputum diminished and became T.B minus on completion of treatment.

6. Radiological:- (figs. 51 & 52).

Note. There is a definite diminution of exudative disease and increase of fibrosis in both upper lobes, particularly in right.



Fig. 51. Before treatment.



Fig. 52. After treatment.

Fig. 51 shows well marked 'fuzzy' active disease in both upper lobes. Fig. 52 shows a marked clearing of the active processes.

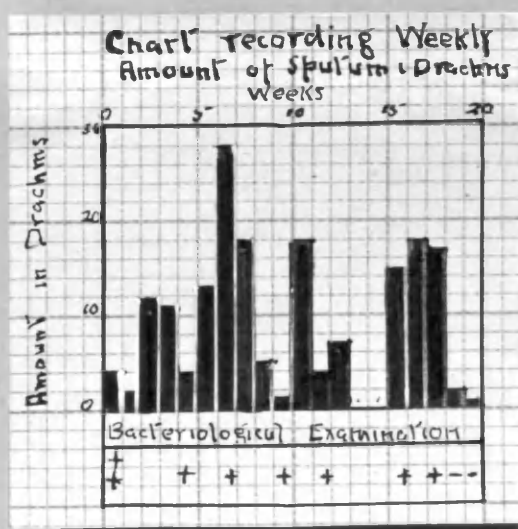


Chart 13.

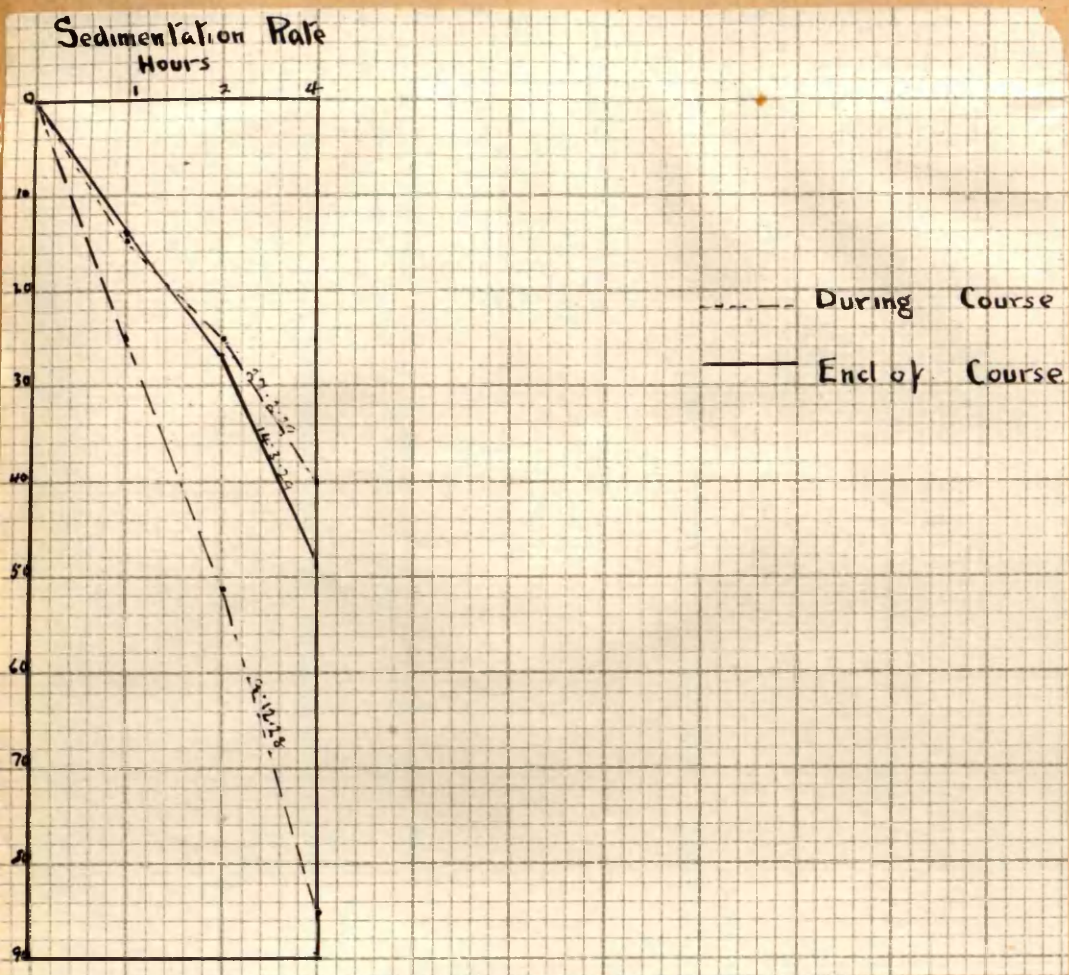


Fig. 53.

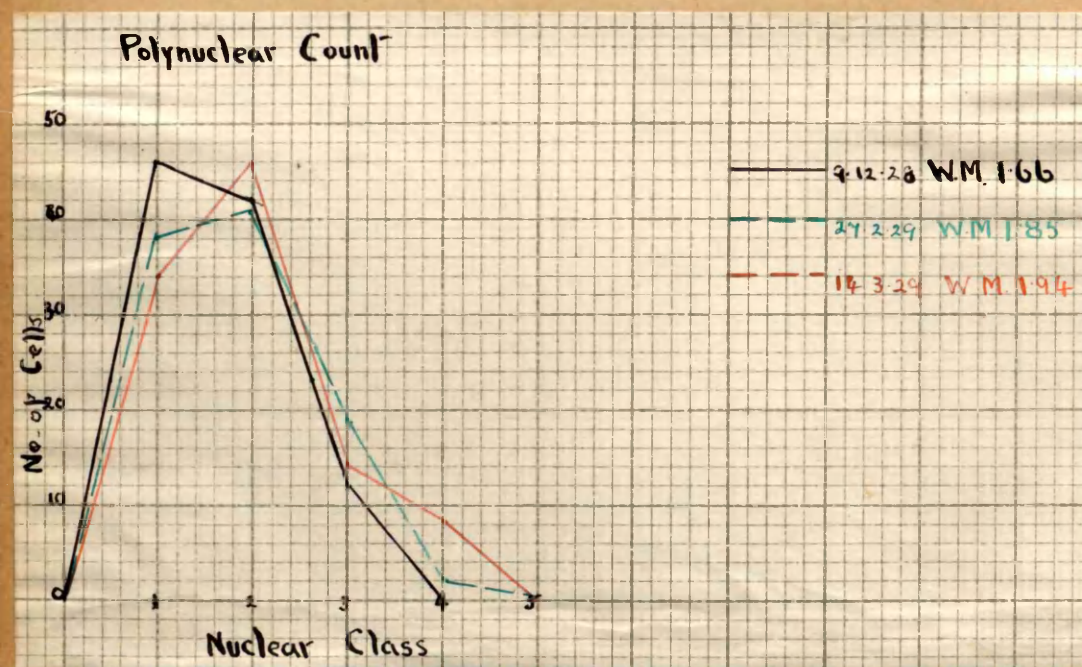


Fig. 54.

7. Physical signs:- P.N. remains impaired over both upper lobes. B.S. are weak on both sides; several fine post-tussive râles are faintly audible at right apex.

8. Red cell sedimentation rate:- (fig. 53).

Note the improvement after treatment.

9. Polynuclear count:- (fig. 54).

Note the right hand drift of the curve on completion of treatment.

Reactions to sanocrysin:- (1) Focal.

#### Resumé.

This patient definitely improved as indicated by the general condition, radiograms and blood controls.

Classified result:- Improved.

## Case 14.

Florence Bates Age 22 years.

Commenced Sanocrysin 31.7.28. Completed 8.1.29.

Duration of disease:- 6 months.

Symptoms:- Cough and spit, night sweats, loss of weight and dyspnoea on exertion.

Patient remained on rest for 9 weeks, and temperature remained febrile, before sanocrysin commenced. Sputum T.B.+++.

Average diurnal temperature:- 97 - 99.

" " pulse rate :- 96 - 116.

Physical signs in chest:- Right side. P.N. markedly impaired over upper and middle lobes. B.S. weak over lower lobe and bronchial breathing over apical region. Numerous medium and fine moist râles present.

Left side. P.N. dull in subclavicular region, with tubular B.S. and whispering pectoriloquy. Crepitant râles present,

Radiogram:- (fig. 55 ).

Classification:- L<sub>2</sub>S<sub>2</sub>+++.

Sanocrysin given:-

•05. •1. •1. •25. •25. •35. •35. •5. •5. •5. •75. •75. •75. •75. •75. •75=8.2 gms

Results of treatment.

1. Average diurnal temperature:- 97 - 98.4
2. " " pulse rate :- 84 - 96.
3. Exercise:- Walks and light ward work.
4. Weight:- Gained 1st. 4 lbs.
5. Sputum:- see chart. 14.

Note diminution in quantity, remains positive although bacilli are scanty.

6. Radiological:- (figs. 55 & 56).

Note the marked radiological improvement after treatment. There is partial resolution of pneumonic area on left side, marked absorption of exudative disease in right upper lobe, and general increase of fibrosis.





Fig.55. Before treatment.



Fig.56. After treatment.

Fig.55 shows a marked amount of active disease in both sides, and defines a pneumonic area in the left side. Fig.56 demonstrates the resolution of the pneumonic area and the marked clearing of active disease in all lobes.

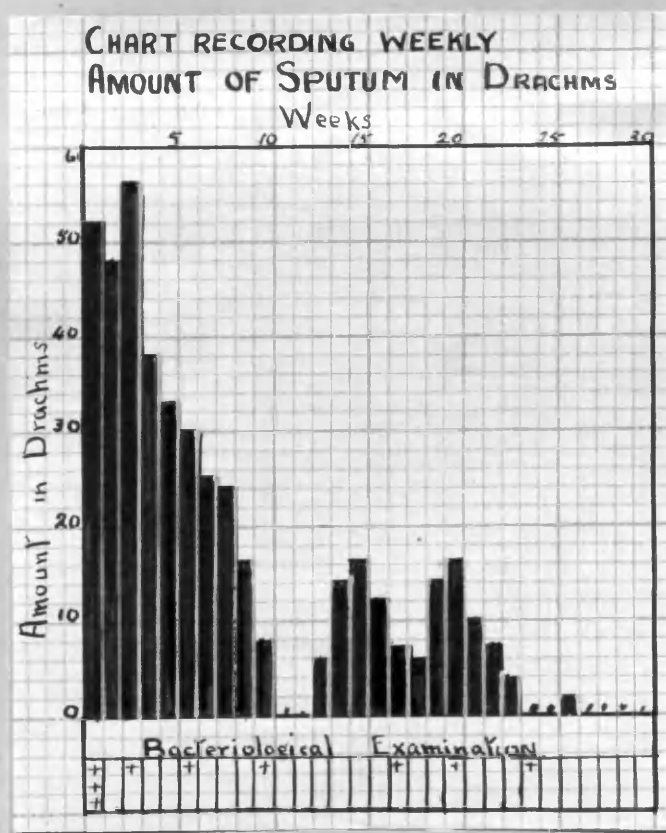


Chart 14.



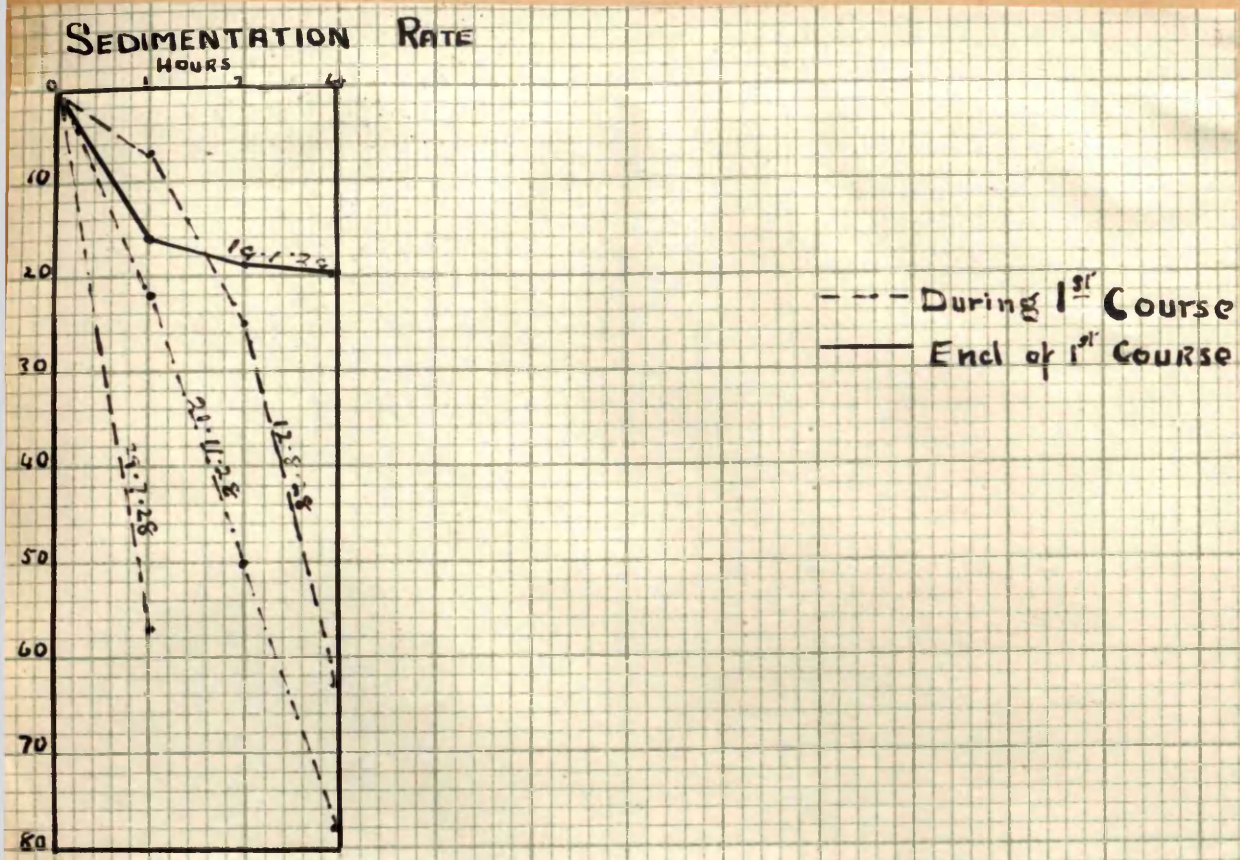


Fig. 57.

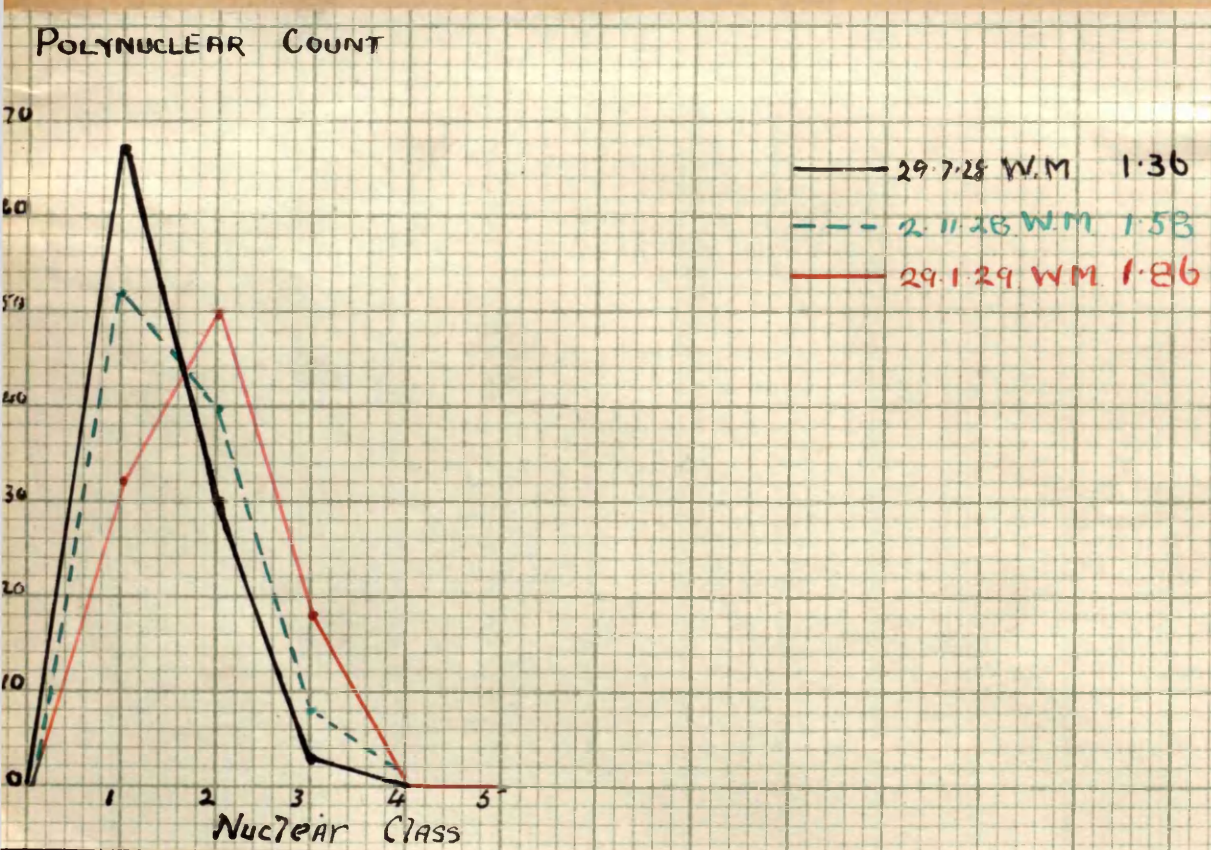


Fig. 58.

7. Physical signs:- Right side. P.N. impaired over upper lobe. Expiration + at apex. B.S. are weak.  
Left side. P.N. almost resonant. Tubular B.S. and crepitations have gone.
8. Red cell sedimentation rate:- Note the steep fall in the 1st hour at the commencement of treatment, and a slight secondary fall in 21.11.28, when the patient was recovering from pleurisy with effusion. The rate at the completion of treatment falls just outside normal limits.
9. Polynuclear Count:- Note the gradual improvement in the curve, but at the completion of treatment it still remains abnormal.
10. Complications:- Pleurisy.
- Reactions to Sanocrysin:- (1) Focal (2) Transient albuminuria.
- Resume

This patient was severely ill before sanocrysin treatment was commenced. She developed pleurisy, and sanocrysin was discontinued for three weeks. She undoubtedly improved, as is evidenced by the absorption of exudative disease, the diminution of sputum, exercise tolerance, and gain in weight. The results of red cell sedimentation rate and polynuclear count, indicate that the prognosis is changed for the good.

Classified result:- Markedly improved.

## Case 15.

Edward Hollingworth age 23 years.

Commenced sanocrysin:- 10.7.28. Completed 20.8.28.

Duration of disease:-

Symptoms:- cough, spit, night sweats, and dyspnoea on exertion.

Sputum:- T.B.+. .

Average diurnal temperature:- 97.4 - 98.8.

" " pulse rate :- 76 - 84.

Physical signs in chest:- P.N. is impaired over both upper lobes where fine post-tussive rales are audible. Air entry is diminished at bases.

Radiogram:- (fig. 59 ).

Classification:- L<sub>1</sub> S<sub>1</sub> +.

Sanocrysin given:- .1, .1, .25, .35, .35, .5 = 1.65 gms.

Results of treatment.

Treatment was discontinued in this case on account of moderately severe dermatitis affecting the face, arms, and trunk. The final radiogram and blood controls were not taken on account of the patient being discharged for misconduct. He remained in bed for 1 month on account of the dermatitis, but subsequently he was able to perform full sanatorium regime, temperature and pulse rate remaining within normal limits. The sputum(chart 15) diminished and bacilli disappeared from it.

Moist sounds disappeared from chest and were replaced by harsh inspiration.

He gained 1st. 9 lbs. in weight.

Classified result:- Improved.



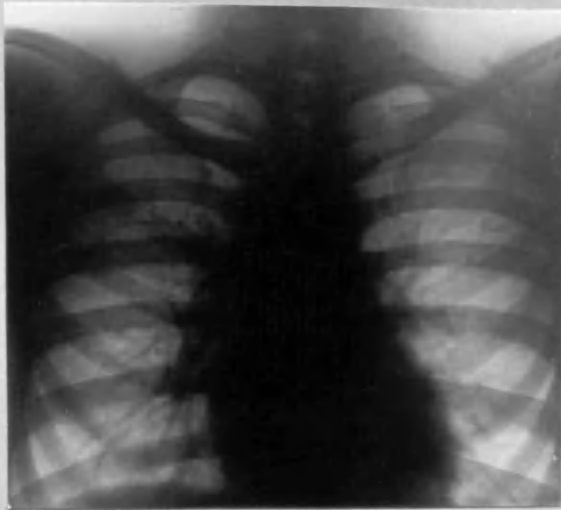


Fig. 59.

The density of the root shadows is increased and there is considerable active nodulation in the right upper lobe.

Chart recording Weekly Amount of  
Sputum in Drachms  
Weeks

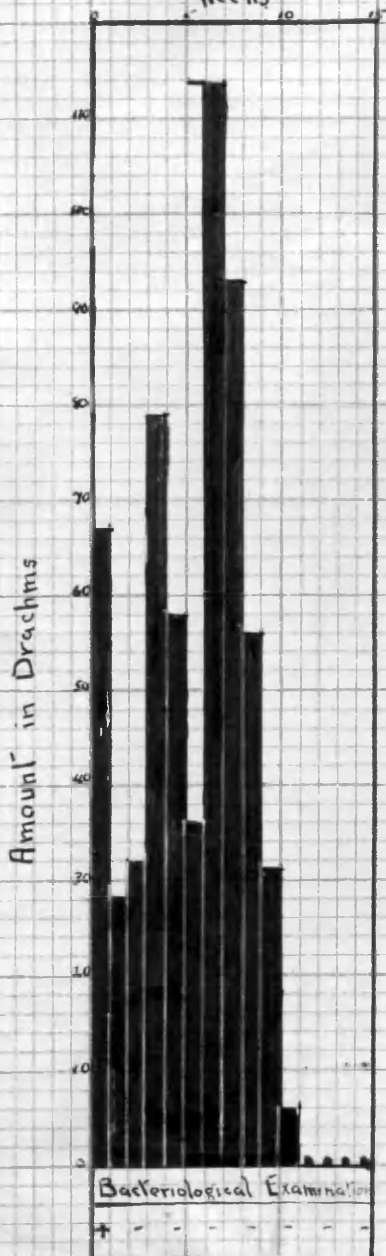


Chart 15.



Fig. 60.

There is extensive active disease in the right side and active nodulation in left upper lobe.

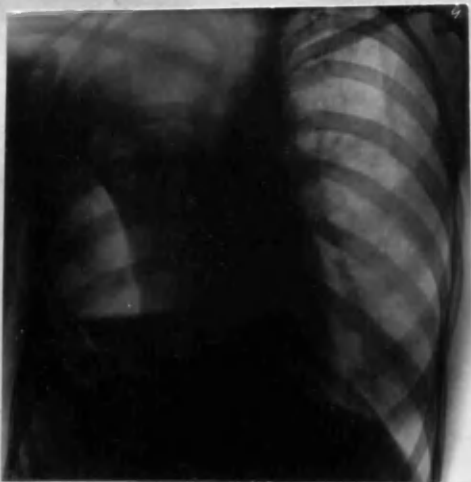


Fig. 61.

This film was taken after air replacement was performed. A line of fluid is still present and the apex of the right lung remains adherent. There is considerable clearing of the active nodulation in left side.

Case 16.

Gladys Challoner    Age 24 years.

This patient was admitted with extensive exudative disease in right side ~~lobe~~ and infiltrative disease on the left ( fig. 60 ). Artificial pneumothorax was performed on the right side, but the apex remained adherent. Sanocrysin treatment was commenced, and 4.37 gms., were given. Sanocrysin was discontinued on account of the development of tuberculous empyema on right side; air replacement was performed. (fig. 61).

The patient's progress was satisfactory until pyopneumothorax supervened, when the temperature became febrile and pulse rate increased.

There is no sputum at present.

She is still under treatment.

Classified result:-    Worse.



## Case 17

Margaret Pipes Age 35 years.

Commenced Sanocrysin. 1st course 9.7.28 Completed 12.9.28.

" " 2nd " 11.12.28. " 31.1.29.

Duration of disease:- 2 months.

Symptoms:- Cough, loss of weight, night sweats, and occasional stained sputum.

Patient had sanatorium treatment for 17 weeks, and temperature remained slightly febrile, before sanocrysin commenced.

Sputum:- none on admission.

Average diurnal temperature:- 97.6 - 99.

" " pulse rate :- 76 - 88.

Physical signs in chest:- P.N. impaired over both apical

regions. Exp.+ on right side, and fine post tussive râles present. B.S. granular over left apex.

Radiogram:- (fig.62).

Classification:- L<sub>1</sub> S<sub>1</sub> 0

Sanocrysin given:-

1st course = .05 .05 .1 .25 .35 .5 .75 .85 .95 .85 .95 = 5.65gms.

2nd " = .1, .25, .5, .75, .75, .85, .85, .85, .85 = 5.75 gms.

#### Results of treatment.

1. Average diurnal temperature:- 97.2 - 98.

2. " " pulse rate :- 74 - 82.

3. Exercise:- full sanatorium régime.

4. Weight:- Lost 5 lbs.

5. Sputum:- no sputum.

6. Radiological:- (figs. 62 & 63).

Note. There is no marked radiological difference after treatment.

7. Physical signs:- P.N. impaired over both upper lobes where expiration is prolonged. No adventitious sounds present.



Fig. 62. Before treatment.



Fig. 63. After treatment.

Fig. 62 shows increased density of root shadows and slight peribronchial infiltration in both upper lobes. There is no striking difference in Fig. 63.

# SEDIMENTATION RATE

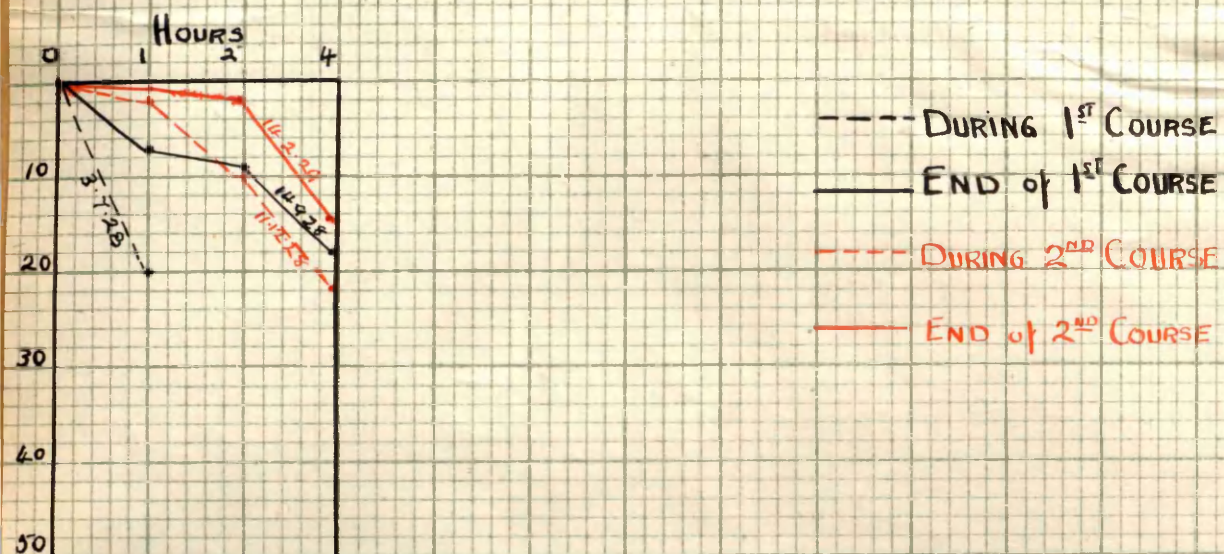


Fig. 64.

# POLYNUCLEAR COUNT

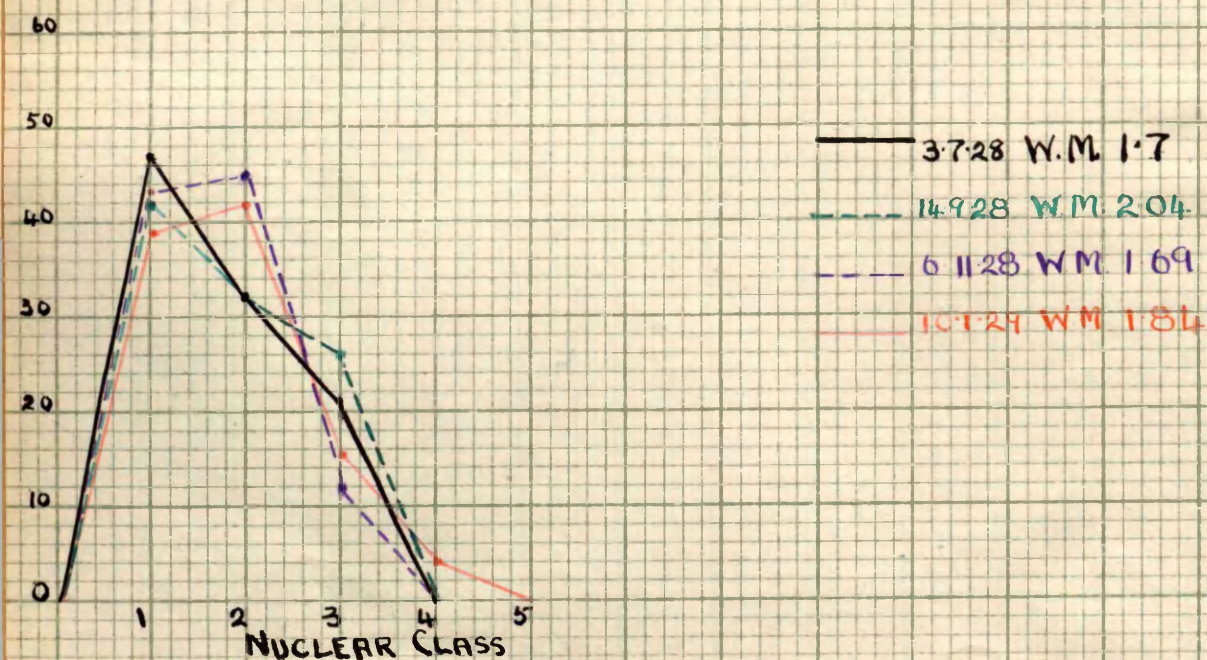


Fig. 65.

8. Red cell sedimentation rate:- (fig. 64).

There is only a slight fall at the end of 1st hour at the commencement of treatment, and the fall progressively decreases to the end of 2nd course.

9. Polynuclear count:- (fig. 65).

There is very slight swinging of the curve to the right after treatment, but the weighted mean still remains abnormal.

Reactions to sanocrysin:- (1) Focal after earlier injections  
(2) Albuminuria.

Resumé.

After treatment this patient was able to perform sanatorium regime without becoming febrile. The improvement is not striking as shown by radiogram, and blood controls.

Classified result:- Slightly improved.



## Case 18

Clara Howes age 27 years.

Commenced Sanocrysin. 1st course 17.7.28. Completed 14.11.28.

" " 2nd " 16.1.29 " 15.2.29.

Duration of disease:- 3 months.

Symptoms:- Cough, night sweats, fainting attacks, loss of weight and slight dyspnoea on exertion.

Had sanatorium treatment for 15 weeks and condition remained unsatisfactory.

Sputum:- Nil.

Average diurnal temperature:-  $97.6 \pm 99$ .

" " pulse rate :- 80 - 90

Physical signs in chest:- Right side. P.N. impaired at apex.

B.S. weak over all lobes. Fine post-tussive rales audible over 'zone d'alarme'.

Left side. P.N. impaired at apex. B.S. are weak and granular over upper lobe.

Radiogram:- (fig. 66).

Classification:-  $L_1 S_2 0$

Sanocrysin given:- 1st course =  $.05, .05, .15, .25, .35, .35, .35, .5, .75, .75, .75 = 4.55$  gms.

" " 2nd " =  $.25, .5, .75, .75, .75 = 3$  gms.

#### Results of treatment.

1. Average diurnal temperature:-  $97.2 - 98$ .

2. " " pulse rate :- 80 - 84.

3. Weight:- Gained 2 lbs.

4. Exercise:- Full sanatorium regime.

5. Sputum:- Nil.

6. Radiological:- (figs. 66 & 67).

There is no significant radiological improvement.





Fig.66. Before treatment.



Fig.67. After treatment.

Fig.66 shows increased density of root shadows on right side and peribronchial infiltration in both apical regions. In fig.67 the radiological structure of the lung is well marked, and there is no definite radiological improvement.

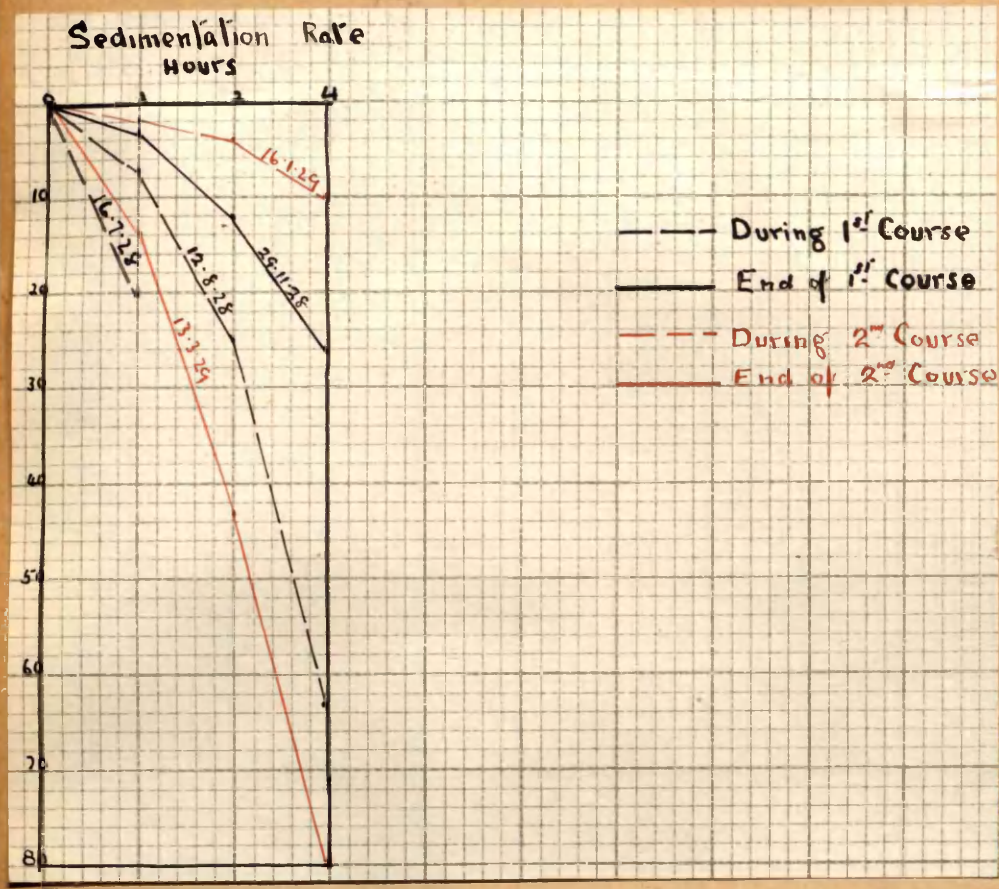


Fig. 68.

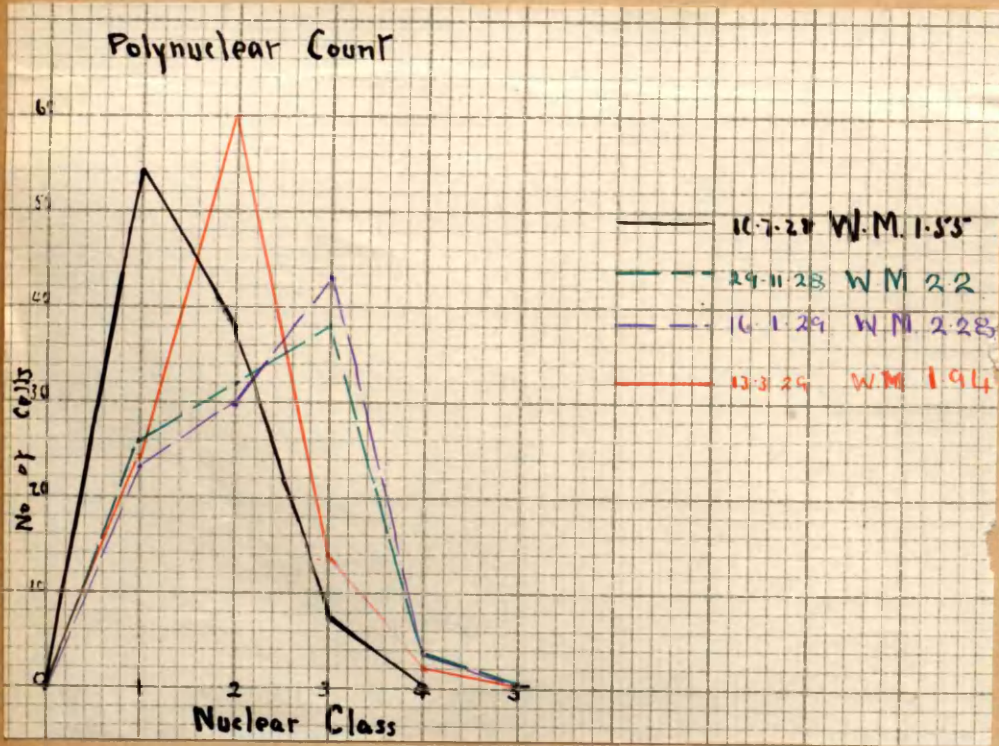


Fig. 69.

7. Physical signs:- P.N. remains impaired at both apices.

B.S. are weak and granular over both upper lobes.

8. Red cell sedimentation rate:- Note the low initial fall, the subsequent improvement, and the retrogression at end of 2nd course.

9. Polynuclear count.

Note the initial improvement and the subsequent drift of the curve to the left at end of 2nd course.

Reactions to sanocrysin:- (1) Stomatitis (2) Transient papular erythema (3) Albuminuria.

#### Resume.

The only improvement in this patient was the exercise tolerance with afebrile temperature. The blood controls suggest that the initial marked improvement was not maintained.

Classified result:- Slightly improved.

## Case 19

Clara Guess, age 18 years.

Commenced Sanocrysin. 1st course 9.7.28. Completed 15.9.28.

" " 2nd " 11.12.28 " 6.2.29.

Duration of disease:- Recent.

Symptoms:- Pains on right side of chest, loss of weight, night sweats, and slight dyspnoea on exertion. Little cough or sputum.

Before sanocrysin treatment commenced, she remained in bed for 30 weeks and temperature remained febrile.

Sputum very scanty and T.B.+.

Average diurnal temperature:- 97.4 - 99.2

" " pulse rate :- 88 - 92

Physical signs:-in chest:- Slight impairment of percussion over both apical regions. Inner borders of Krönig's areas blurred on both sides. B.S. weak and granular over both upper lobes. Air entry markedly diminished on right side.

Radiogram:- (fig.70).

Classification:- L<sub>1</sub>S<sub>2</sub>+

Sanocrysin given.

1st course:- .05 .05 .1 .25 .35 .5 .75 .85 .85 .85 .85 .85 = 6.3gms

2nd " = .1 .25 .5 .75 .75 .85 .85 .85 = 5.65 gms.

#### Results of treatment.

1. Average diurnal temperature :- 97 - 98.4
2. " " pulse rate :- 80 - 84.
3. Exercise:- Full sanatorium régime.
4. Weight:- Gained 4 lbs.
5. Sputum :- See chart 16. Note that sputum disappeared.
6. Radiological:- (figs.70&71).

Note. The nodules in left upper lobe appear less woolly, but film is taken with a harder tube which might account for the difference.



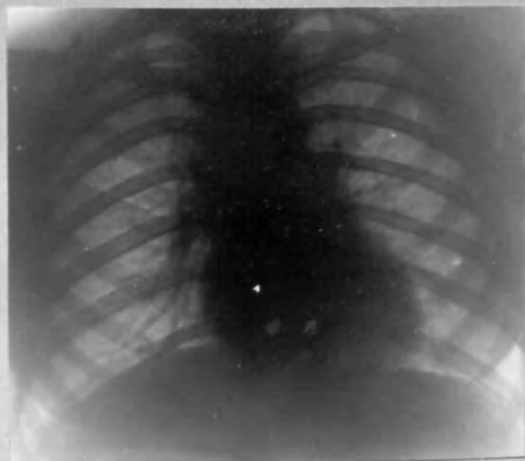
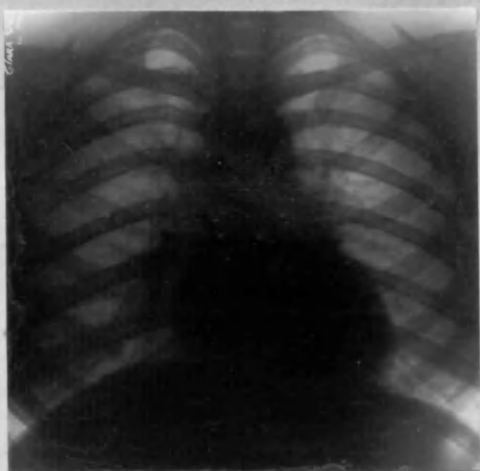


Fig. 70 Before treatment.

Fig. 71. After treatment.

Fig. 70 shows increased density of root shadows & peribronchial infiltration in both upper lobes. Fig. 71 demonstrates that there is no obvious radiological improvement after treatment.

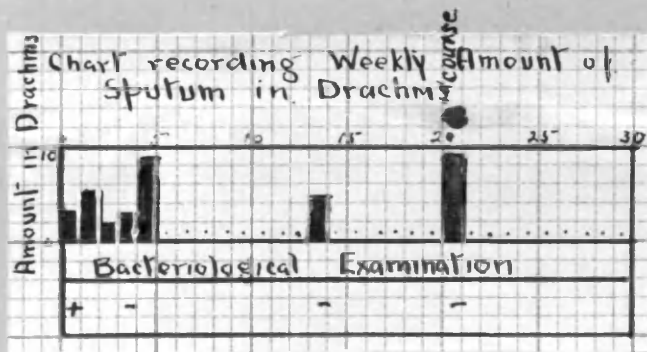


Chart 16.



# SEDIMENTATION RATE

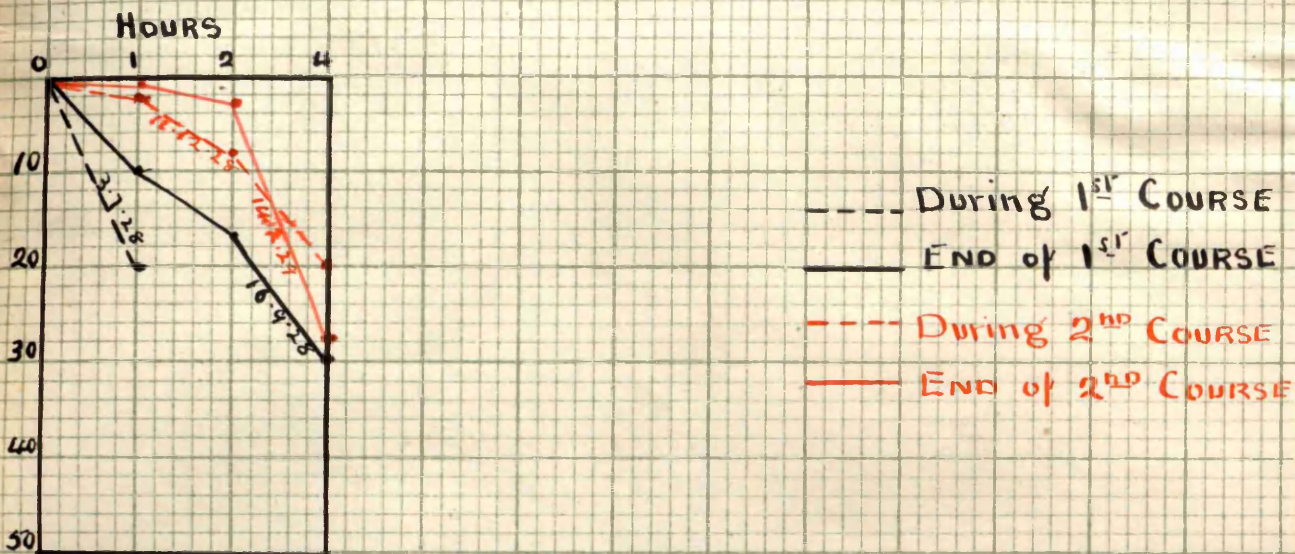


Fig. 72.

# POLYNUCLEAR COUNT

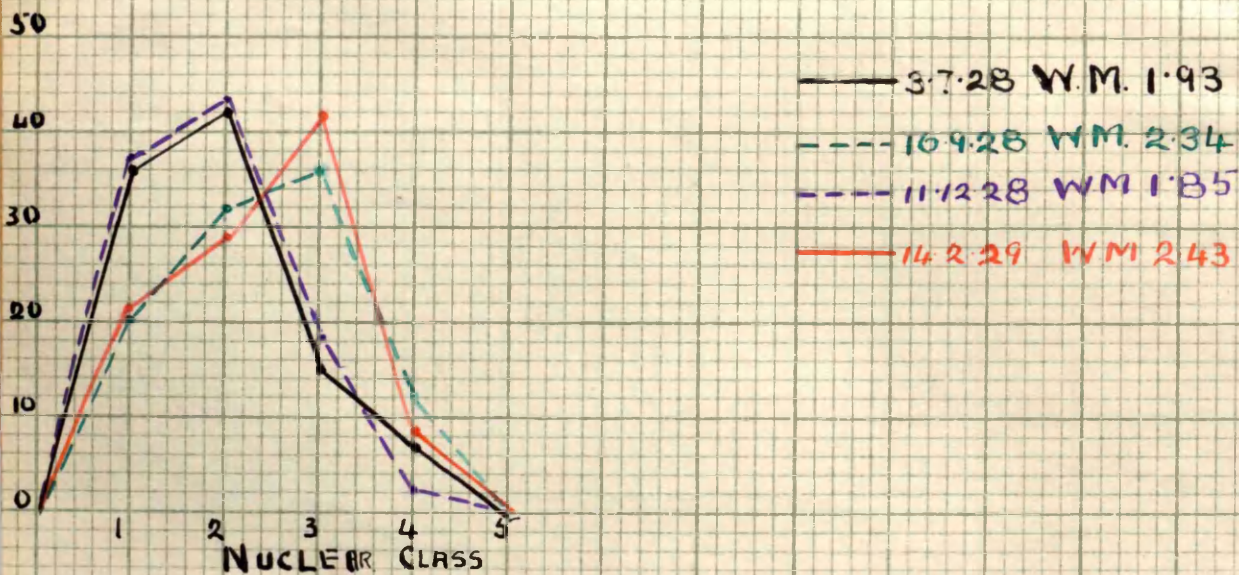


Fig. 73.

7. Physical signs :- No marked change. B.S. stronger, and rather harsh over upper lobes.
8. Red cell sedimentation rate :- (fig.72) Note that the initial fall is moderate, and the rate is very slow at the completion of treatment.
9. Polynuclear count :- (fig.73) Note that the curve swings over to the right at the end of 1st course, but returns to the left at the commencement of 2nd course.

At the end of treatment, the curve is practically normal.

Reaction to Sanocrysin :- Focal.

#### Résumé of results.

Condition improved after 1st course, temperature became afebrile, and she was able to carry out sanatorium régime. On readmission for 2nd course, the improvement was not maintained, temperature was febrile, and she was slightly toxic, as is evidenced by the deviation of the polynuclear curve to the left. The prognosis, however, remained good as the red cell sedimentation rate indicates.

Her condition rapidly improved on the 2nd course.

Classified result	Improved.
-------------------	-----------

61.  
Case 20

Wm. Wignall Age 31 years.

Duration of disease:- 2 months.

Symptoms:- Cough and blood-stained spit, loss of weight, night sweats, pains in chest, dyspnoea and husky voice.

Sputum:- T.B.++.

Average diurnal temperature:-  $98.4 - 101$ .

" " pulse rate:-  $90 - 104$ .

Physical signs in chest:- P.N. impaired over both upper lobes.

Exp. + and crepitations are present over impaired area.

Radiogram:- (fig. 74 ).

Classification:-  $L_3 S_3 ++$ .

Sanocrysin given:-  $.05, .05, .05 = .15$  gms.

Results of treatment.

This patient had a history of short duration, the disease being very acute. The temperature rose to  $102^{\circ}$  immediately after injections, and maintained that level until he died six weeks after commencement of treatment.

Classified result:- Worse.

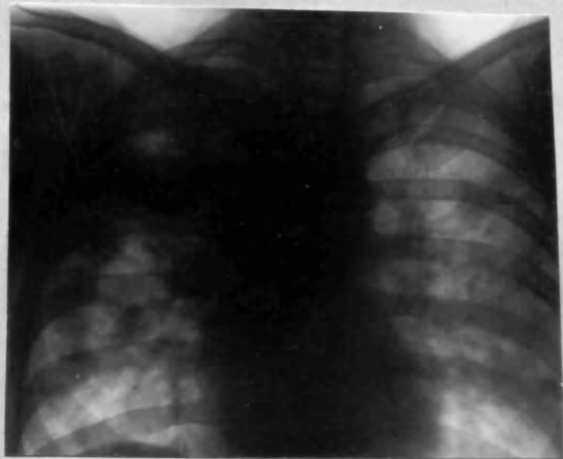


Fig. 7h.

Note the extensive active disease in all lobes.





Fig. 75.

Note the large cavity in right upper lobe and the extensive active disease in left side.



Case 21.

Douglas Mortimer Age 19 years.

Duration of disease:- 2 years.

Symptoms:- Cough and spit, night sweats, loss of weight, pains in chest, dyspnoea and frequent haemoptyses.

Sputum:- T.B.+++.

Average diurnal temperature:- 97 - 99.6.

" " pulse rate:- 96 - 104.

Physical signs in chest:- Right side. P.N. impaired over all lobes. B.S. bronchial over upper lobe.

Numerous crepitations audible.

Left side. P.N. impaired over all lobes. Exp.+ and numerous crepitations audible.

Radiogram:- (fig. 75 ).

Classification:- L<sub>3</sub> S<sub>3</sub> +++.

Sanocrysin given:- .05, .1, .1 = .25 gms.

#### Results of treatment.

This patient had advanced disease. After last injection the temperature shot up to 102°, with the appearance of a brilliant morbilliform rash, which faded in 14 days time. Sanocrysin was discontinued, but his temperature remained febrile. He continued to lose weight, and died three months later.

Classified result:- Worse.

## Case 22.

Alfred Knight age 17 years.

Commenced sanocrysin. 1st course 25.7.28. Completed 30.10.28.

" " 2nd " 27.12.28. " 25.2.29.

Duration of disease:- 18 months.

Symptoms:- Persistent cough and spit, loss of weight and small haemoptyses.

Sputum:- T.B.+++

Patient treated on general sanatorium principles, but showed no improvement. Temperature remained unsettled and sputum blood stained.

Average diurnal temperature:- 97.8 - 99.4.

" " pulse rate :- 96 - 100.

Physical signs in chest:- Right side. P.N. markedly impaired over upper lobe. B.S. vesico-bronchial at apex, VR++, and crepitant râles present over impaired area  
Left side. P.N. markedly impaired to level of scapular spine. B.S. amphoric over impaired area where numerous crepitations and rhonchi are audible.

Radiogram:- (fig. 76).

Classification:- L<sub>3</sub> S<sub>2</sub> +++.

Sanocrysin given:- 1st course = .05, .1, .1, .25, .25, .25, .5, .5, .75, .75, .85, .85, .85 = 6.05 gms.

" " 2nd " = .1, .25, .35, .5, .75, 1, 1, 1 = 4.95gms

Results of treatment.

1. Average diurnal temperature:- 97.4 - 98.4.
2. " " pulse rate :- 84 - 90.
3. Weight:- Gained 1 st. 4 lbs.
4. Exercise:- Walks and light ward duties.
5. Sputum:- see chart.17.

Note the marked diminution of sputum and bacilli. Sputum is occasionally blood stained.

6. Radiological:- (figs.76 & 77).

Note in the right upper lobe, the absorption of exudative disease, and shrinkage of cavity. On the left side there is diminution of active nodulation and increase of fibrosis.

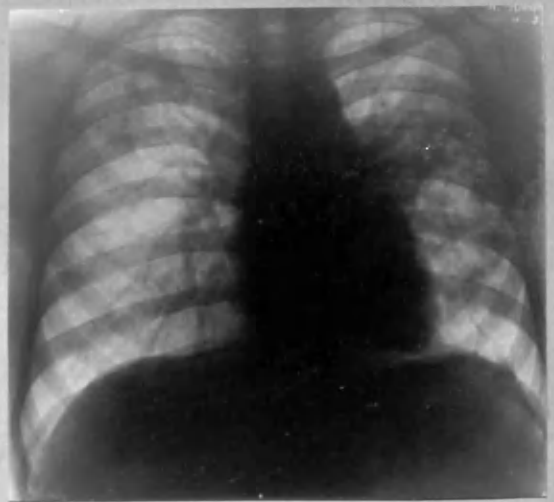
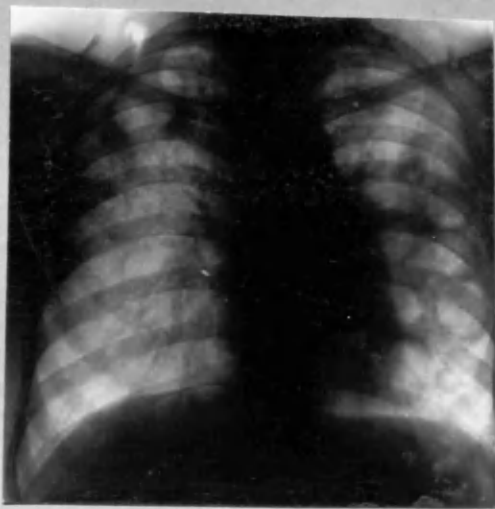


Fig. 76. Before treatment.

Fig. 77. After treatment.

Fig. 76. shows cavitation in right apex and left lower lobe. There is considerable exudative disease in all lobes. Fig. 77 demonstrates shrinkage of cavities, clearing of active disease, and increase of fibrosis over the areas indicated.

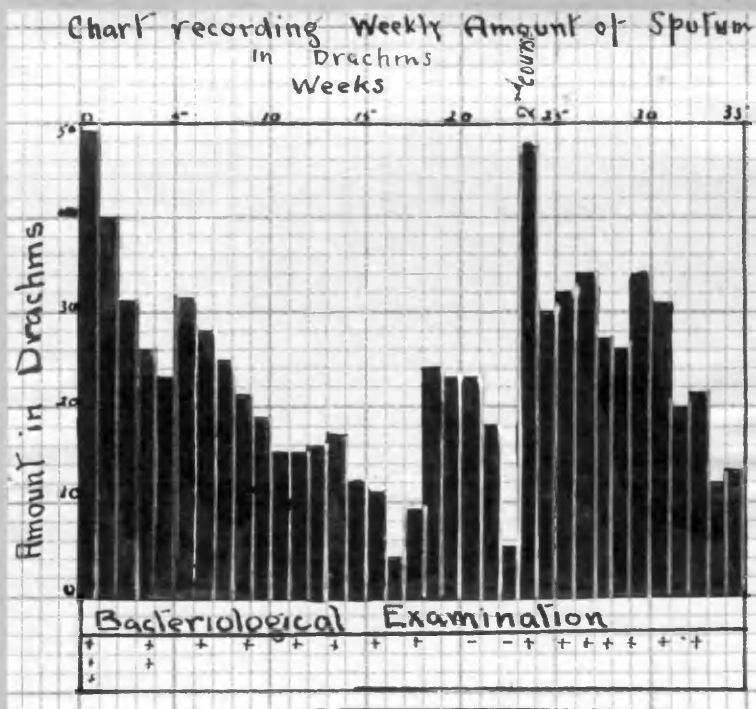


Chart 17.



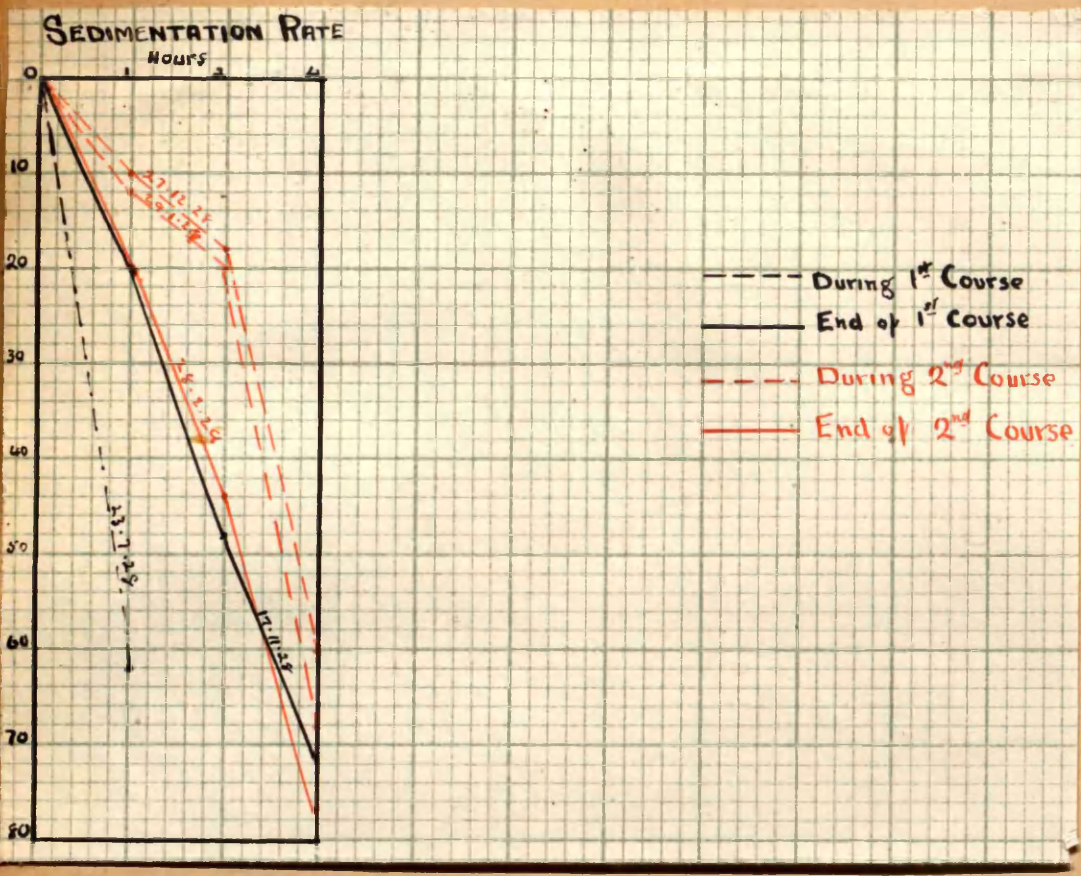


Fig. 78.

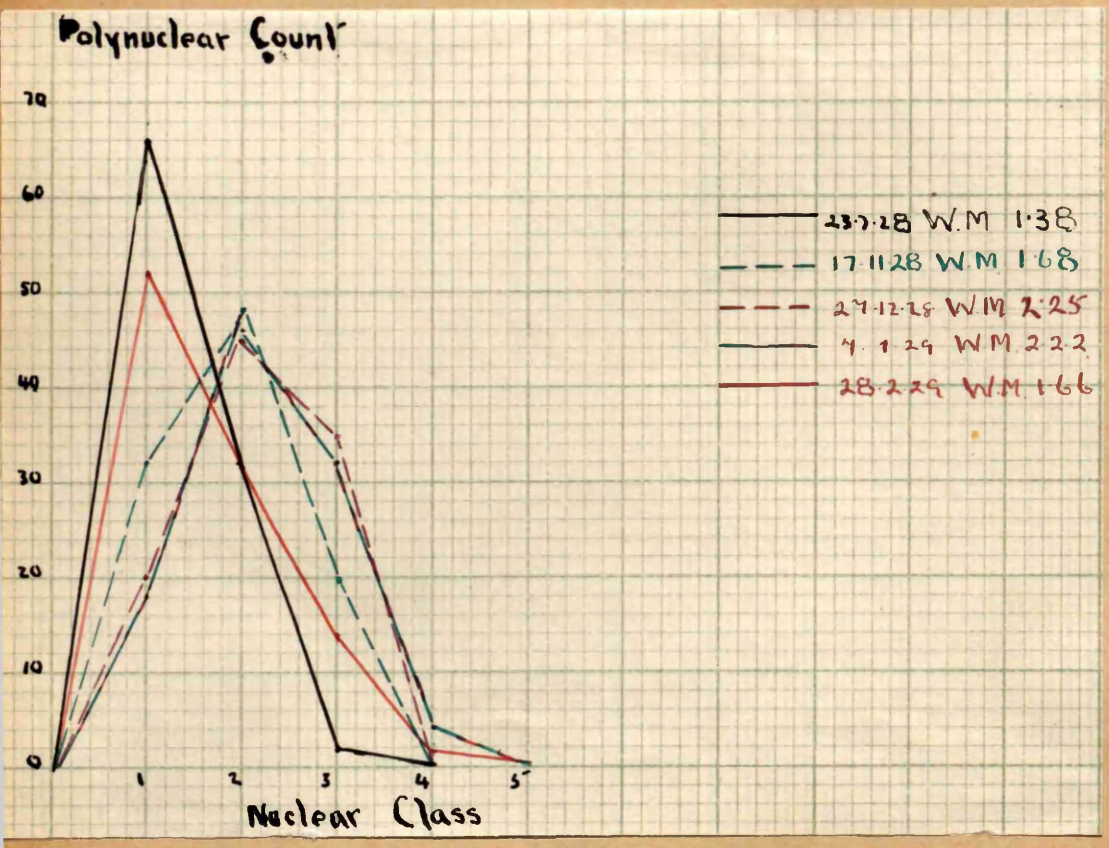


Fig. 79.

- 61
7. Physical signs:- Right side. P.N. slightly impaired over apex. Expiration is prolonged and no adventitious sounds are present.
- Left side. P.N. remains impaired over upper lobe. Expiration is prolonged; amphoric B.S. have disappeared. Crepitations are still present.
8. Red cell sedimentation rate:- There is an improvement in the rate at end of 1st course. During 2nd course the rate still further improves, but falls on completion of treatment.
9. Polynuclear count:- Note the gradual swinging of the curve over to the right until the completion of treatment on 28.2.29, when the curve takes a marked drift over to the left.

Reactions to sanocrysin:- Focal.

Resumé.

In this case there is marked improvement in the radiograms, the physical signs, the temperature and exercise capacity, the sputum and weight. The results of the sedimentation rates and polynuclear counts show that the patient improved up to the completion of treatment, when there was a marked falling away. On this account the prognosis should be guarded. However, there is no doubt that he improved under treatment.

Classified result:- Improved.







(e) Reactions to sanocrysin.

With the individualised dosage employed in the present investigation, no serious reactions were encountered; two cases of mild dermatitis, which cleared up in a few weeks, being the only complications which gave rise to any trouble. The dreaded phenomenon of shock, a frequent reaction in the early clinical trials where the larger dosage was employed, did not arise, and Moellgaard's serum was dispensed with.

The reactions which occurred may be considered as

1. General, 2. Focal.

1. General Reactions.

Immediately following the injections, particularly when the maximum dose was given, the patient felt a metallic taste in the mouth and complained of nausea. Vomiting and looseness of the bowels for a few days were symptoms which occurred in several cases. This mild diarrhoea has been attributed to the excretion of gold by a sensitive intestine.

A febrile reaction was a constant factor in all cases, the temperature rising in the evening of the day of injection, usually subsiding on the day following the injection, and seldom lasting longer than three days except when associated with a complication. The rise of temperature seldom exceeded 101°, commonly between 99° and 100°. The degree of temperature reaction diminished when the same dose was repeated, but increased on increasing the dose. Fig. 80 the temperature chart of case (10), illustrates the febrile reaction which occurred in the majority of cases. In cases where exanthemata occurred, the febrile reaction was protracted even before the rash declared itself.

In the present investigation the following skin reactions occurred.

Morbilliform rashes	-	2 cases
Papulo - erythema	-	3 "
Mild dermatitis	-	2 "

The morbilliform rash appeared early in the course of treatment, lasted a week and disappeared spontaneously. This rash is similar to that obtained in a tuberculin reaction, and Moellgaard maintains that it is caused by the liberation of toxins on the disintegration of the bacilli, which is produced by the specific bactericidal action of sanocrysin.

The mild dermatitis commenced as an ordinary exanthem, became papular on the arms and chest, and ultimately formed a weeping surface with considerable crusting. The condition, however, was mild, and disappeared in a few weeks under treatment with 10% Sod. Thiosulphate intravenously.

The papulo erythema commenced round the elbows and it was difficult at first to decide if the condition would progress to dermatitis. Subsequent injections were delayed, but the lesions were apparently unaffected by the continuation of treatment.

The exact causation of these latter skin conditions is not quite clear. Moellgaard maintains they are toxic in origin, while other workers think they are evidence of a metallic poisoning, comparable to the skin conditions found in arsenical poisoning in the treatment of syphilis. The latter explanation appears more feasible.

Albuminuria occurred in 13 cases. In 2 cases it occurred early in the course of treatment and was associated with exanthemata. In 11 cases the albuminuria occurred in the latter part of treatment when the larger doses were being given. The condition did not give rise to any anxiety and disappeared spontaneously in four or five days. It was observed that the reaction did not reappear when the same dose

was repeated several times, but occasionally returned when the dose was increased. Moellgaard maintains that this reaction is produced by the liberated tuberculous toxin, and he thinks that the gradual disappearance of albumen is due to the increased resistance of the organism produced by active immunisation. He also maintains that albuminuria is made to disappear by the injection of immune serum, but this has not been corroborated by other workers.

The other explanation is that the reaction is due to the irritant effect of the gold excreted by the kidneys.

Stomatitis occurred in 5 cases after the larger doses. The ulceration increased if an injection was given before the mouth had properly healed and on this account treatment was considerably delayed in these cases. The reaction appears to be due to metallic poisoning, and prophylactic measures were attempted by careful attention to the hygiene of the mouth.

During the 2nd course of treatment reactions were the exception, albuminuria and stomatitis only occurring in 1 case.

## 2. Focal.

Focal reactions occurred in all cases immediately after injections. They were evidenced by an increased amount of expectoration, and an increase in the moist sounds in the chest. The reaction subsided in several days, reappeared on increasing the subsequent dose, and did not occur if the same dose was repeated several times.

### Resume of reactions.

Mild dermatitis:- 2 cases

Morbilliform rash:- 2 cases

Papulo-erythema:- 2 cases

Albuminuria      Early:- 2 cases

                    Late:- 11 cases

Stomatitis:- 5 cases.

## Section VI.

### Summary and Conclusions.

The difficulty in assessing the value of any treatment for tuberculosis is well known. Many claims of brilliant results have been made in the past for innumerable preparations, but the vagaries and uncertainties in the progress of the disease make it difficult to dogmatise on the results of any form of treatment. The fallacies of 'post hoc ergo propter hoc' require the fullest consideration before a valid estimate can be made of the value of sanocrysin treatment in tuberculosis.

In summing up the results of sanocrysin treatment, the benefit which may accrue from any concurrent treatment must have due consideration, but the value and limitations of rest therapy and sanatorium regime are now well recognised, and the patients in the present investigation had failed to respond to these measures. In classifying the results of the present investigation an attempt has been made to keep the classifications as simple as possible, to weigh up the results of the various controls, and to give a true estimate of the value of sanocrysin in each case.

The following classifications have been employed;

1. Markedly Improved:- This class includes cases in which improvement was remarkable; the same result could never have been achieved by ordinary routine measures.
2. Improved:- This class includes cases which made a decided improvement; an improvement which might have been accomplished by prolonged sanatorium treatment.
3. Slightly Improved:- This class includes cases in which sanatorium treatment might have achieved the same



result. The majority of cases which come into this classification, however, made a marked initial improvement which was not maintained.

4. Worse:- Cases in which the morbid process was activated by treatment.

The following figure illustrates the classified results of treatment.

	Number of cases	Worse	Slightly Improved	Improved	Markedly Improved
Group I.	4	0	2	2	0
Group II.	14	0	0	8	6
Group III.	3	2	0	1	0
Group IV.	1	1	0	0	0
Total	22	3	2	11	6
%		13%	10%	50%	27%

Fig. 81.

It will be noted from the above table, that 77% of the patients improved, 27% of which markedly improved. This result is most satisfactory. The most striking result is the 100% improvement in Group II cases, 8 cases improving, and 6 cases showing marked improvement. This result is even more remarkable when we appreciate that these cases had active and progressive disease, and having failed to respond to the ordinary routine measures, were on the verge of going downhill. A common feature of the 6 cases which markedly improved, was the resolution of a pneumonic area.

The results in Group I cases are disappointing, considering that they are cases with little tissue destruction although apparently infected with a virulent strain of tubercle bacilli, and presumably the ideal cases for the employment of bactericidal chemotherapy. The satisfactory point about this group is that after treatment, all cases were able to carry out full sanatorium regime,

although there is evidence from the blood controls in 2 cases that the ultimate prognosis must be guarded.

These latter cases have been classified 'slightly improved'.

Of the cases in Group III, 2 died; they were acute cases with a hopeless prognosis, and sanocrysin apparently accelerated the morbid process. The remaining case of this group made a remarkable recovery, but the blood controls on completion of treatment suggest that the disease may readily flare up into activity, and on this account he has been classified 'improved' in lieu of 'markedly improved'. However, the fact remains that this patient is able to carry out full sanatorium régime with afebrile temperature and normal pulse rate; the value of sanocrysin appears to have been in arresting the further spread of disease and giving the existing lesions a chance to heal, while the organism acquired some resistance to the infection.

It is unfortunate that the artificial pneumothorax case in Group IV developed pyopneumothorax while under treatment, because this type of case promises to become amenable to sanocrysin therapy. The patient had improved up to the time pyopneumothorax developed.

#### Special features.

1. Sputum:- It will be noted from the sputum charts accompanying each case, that the sputum diminished after treatment, and in 11 cases it disappeared completely. Tubercle bacilli greatly diminished in numbers, and in some cases the sputum became T.B.- in the early part of treatment, but bacilli returned in the latter part. It is interesting to note that bacilli constantly persisted in the sputum in those cases where there was evidence of cavity formation.

2. Radiological:- The radiological improvement is one of the most striking features of this investigation. The reproductions do not show to the same advantage the improvement which is evident in the original films. The improvement is undoubtedly more marked after the 2nd course. The salient points are clearing of the 'fuzzy' exudative nodulation and increased definition of the fibrotic lesions. In this connection three points require recording.
- (a) The remarkable resolution of pneumonic area. This is well exemplified by 4 cases in Group II.
  - (b) Clearing of active processes which are superimposed on fibrotic lesions. In some cases of this type the contour of cavities become well defined.
  - (c) In a few cases there is definite evidence of shrinkage of cavities, e.g., Cases 10 and 22.
3. Blood Controls:- The blood controls have been a sensitive guide to the patient's condition, and have been of great service in estimating the results of treatment. The controls, on the whole, have been in accordance with the other findings. In several cases the blood findings at the end of 2nd course indicate that the initial improvement has not been maintained; in these cases the prognosis should be guarded, and this has been duly considered in classifying the case.
4. Physical signs:- With the focal reactions there was an increase of the moist sounds which progressively diminished as the treatment continued, and on completion of treatment moist sounds had cleared up in the majority of cases.
5. Weight:- In all cases there was a loss of weight

following the earlier injections, but with the individualised dosage this was soon overcome, and in the latter part of treatment weight was gained. There was rapid gain in weight on cessation of injections, and it was noted that patients on readmission for 2nd course, had gained weight from the time of their previous discharge.

### Conclusions.

It is now six years since sanocrysin was introduced to the medical world and its action is not yet understood. The varying results of experimental work have lead to confusion and uncertainty, but the more recent work tends to disprove Moellgaard's claim for bactericidal specificity. We must, however, bear in mind that a similar position arose in the early experimental work with salvarsan in the treatment of syphilis. Amongst the numerous considerations in unifying the results of treatment in a disease like tuberculosis are the dosage employed and the type and extent of the disease. However encouraging the results of laboratory and animal experimentation may be, clinical investigation is the crucial test in elucidating the indications and contraindications for treatment, the dosage to be employed and the type of disease for which it is most suitable.

The present work deals only with the early results of sanocrysin treatment. Whether the high percentage of improvement will be maintained, is a matter which only time can tell. We can, however, from the results of the present investigation formulate the following conclusions.

1. Sanocrysin, in individualised doses can be used in the treatment of pulmonary tuberculosis without provoking dangerous reactions. Reactions which do occur are mild and when treated promptly are of no significance.
2. Acute toxic tuberculosis is a contra-indication to sanocrysin treatment, due to the extreme poisoning which results from the liberation of tuberculous toxin.
3. The type of case which reacts most favourably to sanocrysin, is that which is classified L<sub>2</sub> S<sub>2</sub>, i.e., a case with considerable amount of active disease in both lungs, which may or may not be superimposed on old fibrotic lesions. This is the type of case which does



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